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THE

AMERICAN JOURNAL

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ORIGINAL ARTICLES

PARTIAL RESECTION OF THE LOWER JAW FOR CANCER.[1]

By Edward M. Foote, M.D.,

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If an operation is only occasionally performed the exact field of its usefulness and the finer points in its technique are more or less forgotten. It is worth while to review such operations from time to time in order to examine their classical descriptions in the light of the present-day practice of surgery. Such an operation is the partial excision of the lower jaw.

This operation is rarely required for trauma, and in cases of osteomyelitis the removal of bone is almost invariably subperiosteal and not, therefore, a true resection of the jaw. It is in the presence of tumors, and especially malignant tumors, that resection of the lower jaw finds its chief use.

I have performed this operation upon fourteen patients in the last three years, and their histories form the basis of a profitable study.

The operation is almost exactly one hundred years old, having been performed for the removal of a new growth by Dupuytren in 1812. Mott, of New York, performed it in 1821, and in February, 1831, Barton published an article in the Amer. Jour. Med. Sci., in which he says: "The records of medicine in this country, as well as in Europe, have already afforded so many examples of the successful removal of large portions of the lower jaw, in cases where the bone had been involved in disease, as to justify and establish the practice in desperate cases, and to require that the operation should henceforth be ranked among those in regular surgery."

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[1] Read before the Clinical Society of the New York Polyclinic Hospital, April 5, 1915.

He illustrated his article by steel engravings of a patient before and after operation, and pictured the saw employed to divide the bone, the instrument being of a type perfectly adapted to the purpose (Fig. 1).

The early operators had as subjects for their skill, patients entirely conscious or partly stupefied with drugs, for anesthetics did not come into practical use much before 1850. The patient was seated in a strong chair and held by main force, although the polite term employed in the description is, "his head was supported by an assistant." The operation was often interrupted by the "restlessness of the patient." The ordeal must have been a severe one for all concerned. It is true that the surgeon was never hampered by an inefficient anesthetist, but that he had other troubles may be seen from O'Shaughnessy's description of an operation performed about 1821.

"Professor Lallemand, of Montpellier, removed a considerable portion of the base of the lower jaw, and when the muscles of the tongue were cut through the patient fell senseless on the floor. The assistants and spectators rushed horror-stricken from the room. The wound was bleeding violently and the greatest consternation and dismay prevailed. The professor immediately applied the actual cautery at a white heat to the surface of the wound, which succeeded in arresting the hemorrhage. He then made an opening into the larynx between the thyroid and cricoid cartilages, through which the air rushed into the trachea, and the patient revived immediately, and ultimately perfectly recovered."

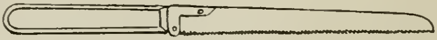

Fig. 1.—Drawing of saw used in 1831 for resection of the lower jaw. (Barton.)

The operation as first performed was commenced by ligation of the common carotid artery, in order to control hemorrhage; but it was soon discovered that this was an unreliable procedure for the purpose and added much to the danger of the operation. It was therefore abandoned about 1820.

From such accounts of operations in the first third of the nineteenth century as I have been able to find, the incision employed ran downward from the mouth to the chin and outward along the base of the jaw. One or more teeth were extracted, sometimes a day or two previous to the operation; though one writer objected to this on the ground that the patient would be less sensible of the pain of their extraction if it were merged in the greater pains of the operation. After the bone was bared in the places selected for its division it was sawed part way through with a small hand saw, or a chain saw; and then its denser portion was divided with cutting forceps.

The incision practised by Cusack, in 1827, is shown in Fig. 2. It would seem that such an extensive incision must surely have produced paralysis of the mouth and lower eyelid, although no mention of this is made in the description of the cases.

Cusack preferred the chain saw, as he found it difficult to protect the soft parts while using a small hand saw, and, moreover, he was often interrupted by the "restlessness of the patient."

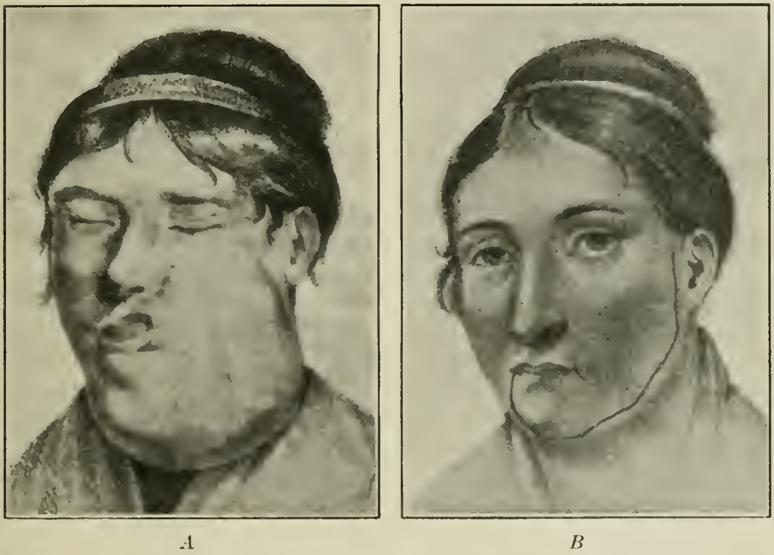

FIG. 2.—*A*, large tumor of lower jaw; *B*, patient after recovery, showing line of incision. (Cusack.)

In Liston's *Practical Surgery*, published in 1837, the incision recommended passed from the condyloid process downward to the angle of the jaw and then forward to the point of the chin. It was then mentioned that to cut through the lip adds to the facial disfigurement, and is in many cases quite unnecessary.

By the latter half of the nineteenth century the operation was so far perfected that the instruments and technique described by Gerich,[2] in 1864, vary little from those employed today. At that time, however, the sitting posture was still advocated to keep the blood out of the throat of the chloroformed patient.

Up to that time a number of incisions had been practised for removal of different parts of the jaw, but the advantages of curved incisions following the lower and, if necessary, posterior margins of the bone were well recognized. Gerich was also keenly alive to the desirability of protecting Steno's duct and as many branches of the facial nerve as possible.

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[2] Ueber Resection des Unterkeifers, Dorpat, 1864.

He pointed out correctly that if an incision along the posterior border of the ascending ramus extends above the level of the lobe of the ear the dissection must be conducted with great care or the branches to the eyelids will suffer; but through an incision no more extensive than this, disarticulation of the bone has often been carried out.

There are three ways, more or less distinct, in which partial resection of the lower jaw may be performed. These are: (1) resection from within the mouth; (2) external resection without disarticulation; (3) external resection with disarticulation.

While all operations for malignant tumors have to be modified to suit the particular case, and partial resection of the lower jaw is no exception to this rule, it is none the less convenient to consider it in these three forms, and to point out under what circumstances each should be employed.

1. Resection performed wholly within the mouth is not suitable for a tumor of the jaw of greater malignancy than an epulis, unless the tumor is a primary one in an early stage, and not involving the bone.

This was the operation performed in three of the cases reported in connection with this paper (Cases II, IX, and XIV). In two of these the tumor was an epulis, and the results of operation were satisfactory even though one tumor was recurrent. In the third the tumor was recurrent and of some degree of malignancy, but, owing partly to a doubtful pathological report, a decision was made to operate within the mouth in defiance of the rule above stated. The continuance of symptoms necessitated subsequent external resection, but the most favorable time for this had then passed.

The technique of resection within the mouth is very simple. An incision is made through healthy tissue completely around the tumor, everywhere down to the bone. With a small chisel and mallet a wedge-shaped piece of bone is chiseled free and removed with the tumor. The gross specimen is examined, and if the tumor is found to involve the bone, or if the cut surface of the bone appears diseased, a deeper layer of bone should be chiseled or gauged away. Nearly the whole thickness of the jaw can be removed without disfigurement or serious permanent injury. In a doubtful case an external resection is usually to be preferred.

Hemorrhage may be controlled with gauze packing. This should be removed daily, as it quickly becomes foul. As soon as granulations are well started no further dressing is needed.

2. External resection without disarticulation of the lower jaw is indicated in all cases of malignant tumors of the jaw itself or of the mucous membrane, or other soft parts close to it, in which there is a fair prospect that the incisions will lie outside of the diseased area. As stated above a resection from within the mouth is permissible for an early epithelioma involving the mucous membrane only.

External resection without disarticulation is more readily performed than resection with disarticulation. It is less dangerous than the latter, and it carries with it less risk of injury to the upper branches of the facial nerve. It is therefore to be chosen for both radical and palliative operations in which the tumor is so situated that the ascending ramus, and the adjacent soft parts are free from disease. Particular attention should be directed to the examination of the parts inside of the mouth, for the region of the pterygoid muscles is a favorite one for extension of a growth situated as far back as the molar teeth. If the disease is in the vicinity of the ascending ramus, disarticulation should be the invariable rule. This is true of even a palliative operation, as the patient will have less pain if the upper part of the jaw is removed.

External resection, in my judgment, is not a good palliative procedure if the disease is so situated that the whole chin would have to be removed; or if as much as one-half of the floor of the mouth is involved, because in such cases the patient is usually more uncomfortable after operation than he was before it. If there is a fair chance of complete removal of the tumor, even these extensive operations may be justifiable; but a most careful examination should be made before they are decided upon. The condition of the floor of the mouth is of the greatest importance in this decision.

The technique of external resection in a simple case is as follows: An incision is made from the point of the chin along the lower margin of the jaw to the angle, and then downward along the sternomastoid muscle to its middle. Skin, fat, and platysma are cut through, the flap dissected downward, the facial artery and vein ligated and divided. The fat, facia, and glands lying between the anterior belly of the digastric muscle and the sternomastoid muscle are dissected free from the hyoid bone upward, and necessary vessels are ligated and divided. The presence of enlarged lymph glands may make necessary a dissection back of the sternomastoid, or as far down as the clavicle. This part of the operation should always be thoroughly done.

If the skin of the cheek is plainly not involved it is dissected upward for an inch or more, care being taken not to injure the upper fibers of the facial nerve. Within the mouth an incision is made wide of the tumor both along the cheek and the floor of the mouth. The external and internal wounds are deepened until they meet on both sides of the jaw, at least at the places at which the bone is to be divided. The cheek can then be retracted upward out of the way of the saw. Any tooth which is in line of an incision through the bone should be extracted, as should be any tooth which will remain close to the incision, for a tooth so situated will become loose and give the patient much annoyance.

One of the best saws for cutting the bone is a small hack saw (Fig. 3). If an instrument maker gets hold of it he is likely to nickel plate it, thereby changing it from a real tool into an ornament. As furnished by the manufacturer it is ready to cut metal, and it cuts the "hardest bone in the body" as an ordinary saw cuts wood.

If the cheek is retracted and a strip of metal like a tongue depressor or a flat blunt scissors is held back of the bone to protect the tongue, the surgeon can work the saw vigorously in short strokes that rapidly eat away the bone. When the bone has been divided the fragment to be removed is held with strong forceps while the bone is sawed in the second place. If a splinter breaks off or the soft parts get in the way the section may be completed with bone shears. The loosened fragment is then turned down and its deep attachments are divided, permitting it to be removed with the mass of glands.

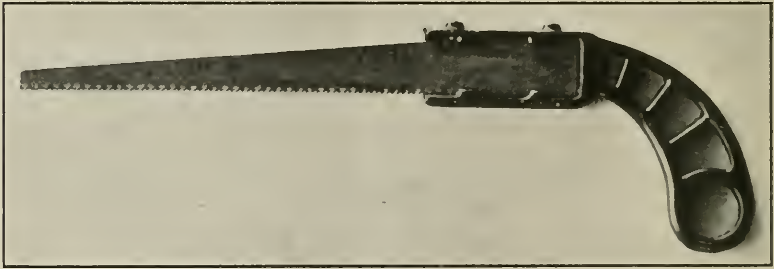

Fig. 3.—Hack saw for cutting jaw bone.

All bleeding is stopped by clamps or hot compresses, for as in all serious operations for malignant tumors the preservation of his blood is the salvation of the patient. Vessels which still bleed are ligated with fine catgut. The wound is carefully gone over. Suspicious spots, whether of bone or soft tissue, are still further excised. The cut ends of the bone are rounded a little with bone shears. Flaps are approximated and sutured both within the mouth and externally, except for about an inch where gauze or rubber tissue drainage is employed. It is desirable to suture the wound in the mouth completely. When this is done primary union often results throughout its greater portion and leakage is slight. If extensive removal of mucous membrane prevents complete suture the internal wound should still be closed as nearly as possible and the remaining gap stopped with the gauze.

Primary union of so much of the external wound as is sutured is the rule, and all stitches should be removed in less than a week. The power of growth of these tissues is tremendous, and even a considerable hole into the mouth rapidly fills in.

Probably for this reason necrosis of the cut ends of the bone is not common. I experienced it only twice after nine external resections without disarticulation (eighteen cut surfaces of bone).

If the growth is so situated that the part of the jaw carrying the incisors must be removed the incision and dissection of the neck as above described should be carried out on both sides to provide for the removal of involved lymph glands.

The chief dangers of this operation are associated with (*a*) anesthesia, (*b*) excessive hemorrhage, (*c*) blood in the throat, and (*d*) falling backward of the tongue when its attachments are severed. These are all real dangers and deserve careful consideration.

(*a*) The ordinary mouth anesthesia is not well adapted to external resection of the jaw, and it adds materially to the risk of operation. Vapor anesthesia through the nose is much better if the patient can be kept under by this method, which is by no means certain. Rectal anesthesia[3] is ideal. If necessary the mask and a little ether or chloroform can be used to put the patient deeply under at the start. After that the anesthetist and his apparatus are entirely out of the way and, more important still, there is no increased mucous and saliva in the patient's throat.

(*b*) Excessive hemorrhage should be guarded against from the beginning of operation. Large vessels should be clamped before they are cut. Smaller ones should be promptly controlled by clamps or pressure. The worst region is below or back of the angle of the jaw, where a large vein may be cut laterally or some branch severed while the tissues are on the stretch. Then when they are relaxed the vein withdraws and a fountain of dark blood wells up from some unseen opening. Pressure on both sides of it to stop the flow, and division of the superficial tissues until the vessel is clearly exposed are the surest ways to meet the difficulty. It is well not to push the deep dissection in this region until the jaw has been cut through twice. The dissection can then be carried from above downward, which lessens the risk of serious venous hemorrhage, and the mobility of the bone makes deep exposure easier.

(*c*) Blood can be kept out of the throat by a good-sized pad of gauze kept in the mouth and changed as often as it becomes saturated. A string through it is a safeguard against swallowing, but a quicker way is to clamp a corner of it projecting from the mouth.

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[3] Ether, 1 ounce by measure to 25 pounds of the body weight, is mixed with paraffin oil in the proportion of two parts of ether to one part of oil. This is injected slowly into the empty rectum one-half hour before operation. A preliminary hypodermic of $\frac{1}{6}$ or $\frac{1}{4}$ grain of morphin is advisable.

(*d*) A heavy thread should always be passed through the tongue either in the middle line or a little to the affected side. It serves to draw the tongue out of the way, and can be used to prevent the loosened tongue from blocking the throat. This accident is more likely to happen the farther forward the excision. If the digastric and muscles anterior to it are divided, the tongue sometimes almost snaps back into the throat. If held forward for a few minutes the tendency grows less as the remaining muscles become accustomed to the change; but such a patient must be watched every minute until he is well out of his anesthetic. I nearly lost one patient from suffocation produced in this way. At the close of operation I left the house surgeon to apply the dressing and went into an adjoining room. In a few minutes I was called back and found the patient black, making no effort to breathe, and almost pulseless. When the bandage was cut off and the tongue pulled forward he still made no effort to breathe, but revived after a few minutes of artificial respiration. One may readily arrange a mechanical contrivance to hold the tongue forward, but it is safer not to leave a patient for a few hours, whose tongue tends to sag back into the throat. During this time the thread should of course remain in the tongue.

3. External resection of the lower jaw with disarticulation is indicated in cases of malignant tumors situated far back in the cheek, or in the jaw bone, and especially if such a tumor is recurrent, for in such a case the involvement of the ascending ramus or of the muscles lying on its inner side may be present to an extent not readily determined by examination of the patient. The technique of its performance is similar to that of external resection. It is therefore only necessary to mention certain differences.

The incision has generally to be extended up in front of the ear a variable distance. It is quite easy to remove a normal jaw without injury to the upper branches of the facial nerve, but a wide excision of soft parts is more important than the preservation of the parotid gland and facial nerve if the tumor involves the ascending ramus or tissues in its neighborhood. Therefore, one should not hesitate to sacrifice these important structures if it seems indicated to gain an increased freedom from recurrence. If the decision is to preserve the parotid gland or the greater part of it the skin incision should not extend above the external auditory meatus and the deeper incision not quite up to this. By dissecting under the parotid, especially in its anterior portion, it will then be possible to lift it and the cheek up and out of the way so as to permit of the disarticulation of the jaw. Before this is attempted the bone should be sawed through anteriorly and the dissection within the mouth completed. The muscles are then divided along the malar bone from in front backward. When the temporal muscle is cut from the condyloid process the fragment of the jaw can be swung outward so as to expose the joint. The rather loose capsule is cut or torn and the bone with the tumor and the attached soft parts are removed. Removal of a part of the parotid gland usually leaves the patient with an external salivary fistula, but this soon dries up if the main duct is not interfered with.

After Treatment. A patient upon whom there has been performed an external partial resection of the lower jaw, with or without disarticulation, should be carefully watched for a few hours to guard against recurrent hemorrhage or a blocking of the throat by the loosened tongue. Some of the patients have great difficulty in swallowing, especially if the dissection has been extended to the anterior pillar of the fauces. This is not to be wondered at when one thinks of the extent of the wound and its close relation to the muscles of tongue and throat.

No nourishment should be put into the patient's mouth until he has shown his ability to swallow water. In severe cases it may be necessary to employ nutrient enemata for a few days or, preferably, to pour fluids through a slender stomach tube passed through the nose and into the esophagus. It is not necessary for the tube to reach the stomach, so that a large rubber catheter may be used if no small stomach tube is at hand. This should be done only twice or three times a day, and a pint or more of water and fluid nourishment poured slowly through it each time.

Most patients swallow readily after two or three days. Only one patient in the present series (Case XI) had a prolonged difficulty in swallowing, and his tumor was so extensive that a part of his pharynx was cut out.

It is a good plan to allow these patients to sit up as soon as they may desire, sometimes after three or four days. They quickly learn to keep the mouth rinsed out, especially after taking nourishment, and if fluids from the mouth render the dressings foul, these should be changed twice daily. Postoperative pain is not as great as one might suppose from the extent of operation. The discomfort of the patient seems to be less than that which follows an excision of the tongue.

Results of Operation. Soon after operation the portion of the lower jaw which remains swings toward the operated side, thus bringing the molars within those of the upper jaw and the incisors back of the upper incisors. Various plans have been suggested to prevent this, two of which are worth mentioning: The upper and lower teeth may be wired together for a few weeks to keep the lower jaw in place while the wound is healing. A prothesis of wire or rubber, or some other non-irritating material, or a strip of live bone, may be inserted between the fragments of the bone after resection without disarticulation.

I have never employed these devices in malignant cases, as I believe their use is not advisable. Wiring the jaws is a dirty and irritating procedure, and the patient needs all the help he can have to keep his mouth in good condition. The use of a foreign body between the fragments is also a source of irritation under circumstances in which an absolute primary union can scarcely be hoped for. Moreover, the possibility of recurrence is so great that the patient must be watched from month to month, and another opertion performed as soon as the tumor shows itself in any part. If a foreign body is present to change the appearance of the wound by its own irritation the early recognition of the new tumor formation is rendered more difficult; and if a second operation proves necessary, the prothesis must, of course, be removed.

It has been suggested to insert a prothesis at a late period, but it is difficult to do this satisfactorily even a year after operation; and a much longer time than that must elapse before one can feel sure that there will be no recurrence. Moreover, in many cases there has been so wide a removal of the soft parts, that only a scar remains in which to bury the prothesis. In other words, the conditions are very different from those which follow the loss of a portion of the horizontal ramus by trauma or inflammation, and in which there has been very little loss of the soft parts.

The decision to reject all foreign bodies in the month after these operations is confirmed by the good functional results which have followed operation in this series of cases, provided the patient has been freed of his malignant disease. Every such patient has good motion of the jaw, and most of them have so developed the lateral motion as to be able to chew on the sound side. One man even goes so far as to claim the operation has cured a long-standing dyspepsia, since now he has to eat more slowly.

Photographs of five of these patients are introduced to show the amount of disfigurement which results from operation and the functional power of the jaw and eyelids.

Late Results. The late results can best be estimated when considered in connection with the character and situation of the growth.

All but one of the fourteen patients operated upon were men.

The ages varied from thirty to seventy-five years, more than half of the patients being between forty-five and fifty-five years old.

As nearly as one could judge the growth started in the jaw (usually in its mucous membrane) in 8 cases; in the lining of the cheek in 3 cases; in the angle of the mouth in 2 cases; while the spindle-cell sarcoma in Case VII seemed to start just below the jaw, possibly from its periosteum.

Nine of the patients had recurrent tumors following operation elsewhere when they first came under my observation. Two presented themselves with primary tumors of the cheek, which I excised without resection. In both of these cases subsequent removal of the bone failed to arrest the growth. In 3 cases resection was the first operation performed, and in these patients no recurrence has showed itself. It is impossible to state positively that a primary resection would have saved the others, but it would certainly have given them a better chance. If anyone thinks that primary resection is unnecessarily mutilating it is only necessary to point out how rapidly a tumor of the cheek can spread in spite of lesser operations, as seen in Cases X and XII.

Of the eleven resections performed for recurrences, four were known to be merely palliative, but even in these cases the operation seemed well worth while, as the patient was given a clean mouth for varying periods of time. Ten resections were performed with the hope of a permanent cure, 3 being primary operations and 7 after recurrences from other operations. One of these patients died from operation and 2 others from recurrences, while the remaining 7 are at present free from recurrence as far as physical examination can show after periods ranging from six to thirty-three months. It is probably too much to expect that all of these patients are cured, but I think we are justified in saying that the prognosis following partial resection of the lower jaw for cancer is more hopeful than it is generally supposed to be.

A summary of these cases is presented on page 24.

Case I.—Male, aged seventy-five years. Disease noticed in the right side of the lower jaw for one and a half years. Operation from within the mouth in Richmond, Va. Recurrence soon appeared, but further operating was discouraged.

Operation at New York Skin and Cancer Hospital April 9, 1912. Resection of two and a half inches of the right side of the lower jaw by incisions within the mouth and below the jaw. The anterior cut near the median line showed the remaining bone to be diseased. The posterior cut was through apparently healthy bone. On account of the age and feeble condition of the patient a more extensive operation was considered inadvisable. The wound in the mouth was entirely sutured, as was the skin wound. Primary union resulted with a minute sinus leading to the anterior cut in the bone.

The patient did well for some weeks; then noticing the recurrence, he consulted another surgeon in Richmond, who removed the chin and part of the left ramus. Patient died from shock in forty-eight hours.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

Case II.—Female, aged forty-five years. Ten months disease existed as a small nodule on the lower jaw opposite the second right bicuspid. After seven months this was removed, with two bicuspid teeth and one molar. In two months recurrence was noticed of a hard, purplish color, with ulceration, at times painful.

Operation at New York Skin and Cancer Hospital July 2, 1912. Right incisors, canine, and second molar teeth were removed. The tumor with surrounding mucous membrane was excised, half or more of the thickness of the jaw bone in its vicinity being chiseled away. The remaining mucous membrane was sutured. The patient recovered promptly.

Two years and nine months later the patient was examined and found free from recurrence.

Pathological diagnosis by Dr. Jessup: epulis, giant-cell sarcoma type. Bone not invaded.

Case III.—Male, aged forty-four years. Growth began as a blister in the right angle of the mouth. Patient was operated upon in ten days at the Long Branch Hospital, and operated upon a second time one year later. There was again a recurrence, with rapid growth. Fifteen months after the tumor was first noticed it extended from the right angle of the jaw to the median line and from the lip to one inch below the lower margin of the jaw.

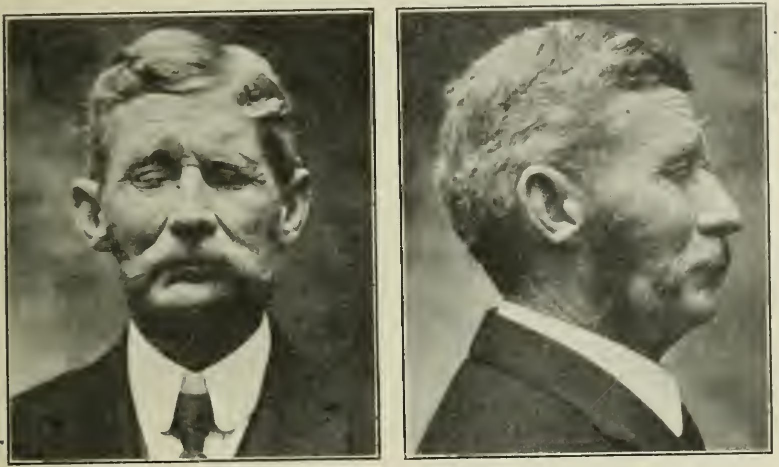
Operation at New York Skin and Cancer Hospital August 1, 1912. Most of the patient's lower lip, his chin, and a portion of the lower jaw measuring two and three-quarter inches, mostly on the right side, were removed, together with the submaxillary gland and enlarged lymph glands. The flaps were undermined and an incision to relieve tension was made through the skin of the right cheek. This permitted a complete suture. Gap in the cheek covered with skin grafts. Wound healed primarily, the skin grafts all taking. Patient discharged in eleven days.

Operation at New York Skin and Cancer Hospital September 24, 1912, for a recurrence in the right cheek about three-quarters of an inch in diameter. Wound healed primarily. One month later patient wrote that his face was smooth and all healed. Five months later recurrence began to trouble him and ten and a half months after resection of his jaw, he died.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

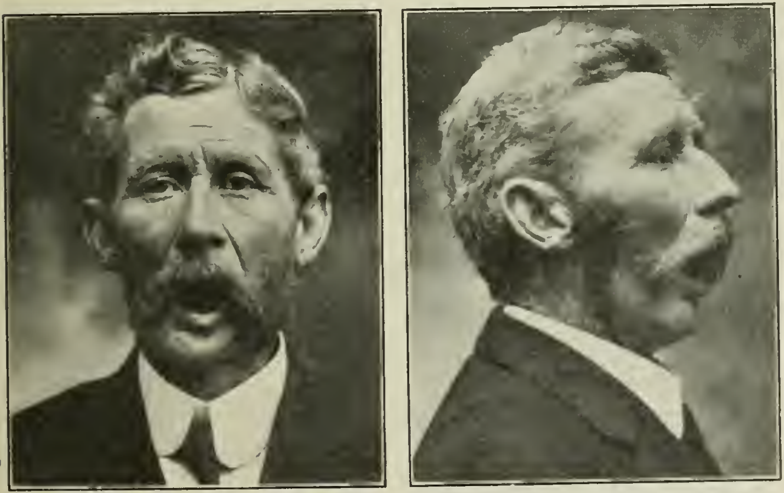
Case IV.—Male, aged fifty-four years. The tumor began in the inner side of the right cheek opposite the second molar. In one year it reached the diameter of about one inch and extended close to the lower jaw.

Operation at New York Skin and Cancer Hospital August 27, 1912. An incision was made across the neck below the jaw and curving upward in front of the ear, also for a short distance down the sternomastoid. The cheek was divided around the tumor. The jaw was cut through back of the bicuspid teeth, twisted out of its articulation, and removed with the tumor and the submaxillary and parotid glands. Branches of the facial nerve to the mouth and eye were divided. Patient was a good deal shocked but recovered sufficiently to leave the hospital in three weeks. Sagging of the lower eyelid gradually became less marked. Two years and eight months after operation there were no signs of recurrence and patient was in good health (Fig. 4).



Front view, mouth and eyes closed.

Side view, mouth and eyes closed.



Front view, mouth and eyes open.

Side view, mouth and eyes open.

Fig. 4.—Patient No. IV, twenty-nine months after partial resection of the lower jaw, with diarticulation, for epithelioma of cheek. Partial paralysis of the mouth and the right eyelids has gradually lessened until the lips open and close almost normally and the conjunctivitis has disappeared.

Pathological diagnosis by Dr. Jessup: epithelioma of the cheek; no invasion of the lower jaw or lymph nodes.

Case V.—Male, aged thirty-four years. A tumor began in the left angle of the mouth and in six months reached the size of the end of a thumb, when a V-shaped portion was excised from the lower lip at Red Bank, N. J. Five months later a mass about one inch in diameter was removed from the lower jaw at Asbury Park, N. J. Three months later another small mass was removed by another surgeon. Recurrence persisted until it involved the left horizontal ramus of the jaw and most of the cheek.

Operation at New York Skin and Cancer Hospital October 10, 1912. An incision was made from the left angle of the mouth backward to the angle of the jaw and a second incision carried backward below the horizontal portion of the jaw. The jaw was cut through at the symphysis and behind the angle. A portion of the cheek between these incisions, the part of the lower jaw indicated, and the glands of the submaxillary region and below the angle of the jaw were removed. The wounds in the mucous membrane and the skin were entirely sutured and healed primarily, except at drain points. The patient did well for some months and died of recurrence nine months after operation.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

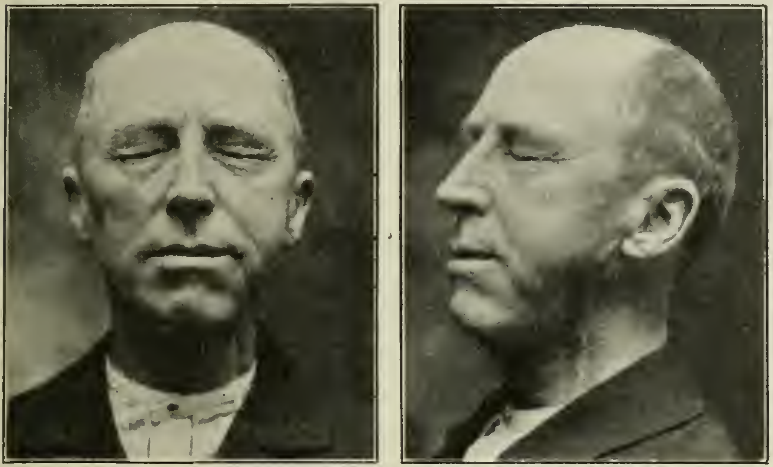
Case VI.—Male, aged fifty-two years. Noticed a tender mass under right side of the lower jaw after doing some heavy lifting. Six months later an enlarged "gland" was removed by his physician. Subsequent growth was rapid, with discharge of pus and blood. One month later a mass three inches in diameter involved the right horizontal portion of the lower jaw.

Operation at St. Mary's Hospital, Jamaica, L. I., June 20, 1913. An elliptical incision was made around the tumor and extended down the side of the neck. The lower jaw was cut through one inch from the median line and one inch above the angle. The mucous membrane was cut through close to the jaw, as it was not involved. The involved portion of the lower jaw with the tumor mass, overlying skin, submaxillary and parotid glands, and numerous lymph glands along the sternomastoid were removed. The wound was entirely sutured externally and within the mouth. The patient collapsed from the extensive loss of blood, but recovered and the wound healed satisfactorily.

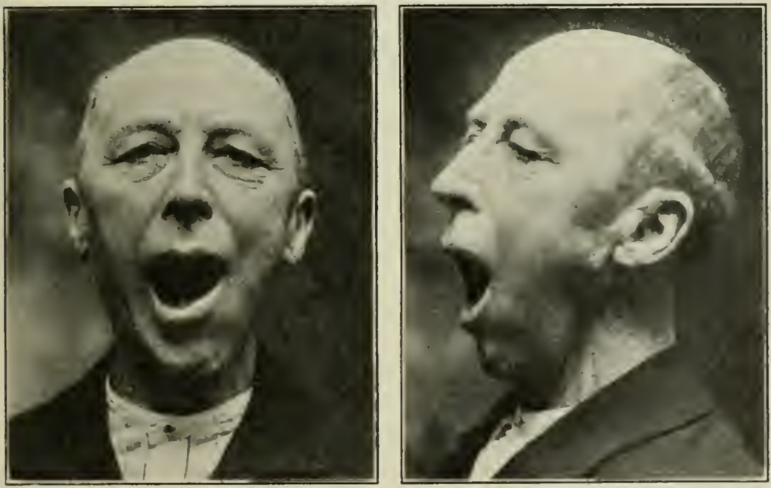
Recurrences in the neck were noticed in about two months, and death occurred four months after operation.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

Case VII.—Male, aged sixty-two years. Was operated upon in East Orange, N. J., in April, 1913, for a movable tumor in the left side of the neck close to the jaw, which had been noticed for six months. The tumor was pronounced a spindle-cell sarcoma. The swelling under the jaw never entirely disappeared, and for four months it seemed to grow more rapidly. Seven months after this operation it measured three inches by two inches and was attached to the jaw and to the skin. Small enlarged glands, freely movable, were felt on the right side in the submaxillary region. The inside of the mouth was normal.



Front view, mouth and eyes closed. Side view, mouth and eyes closed.



Front view, mouth and eyes open. Side view, mouth and eyes open.

FIG. 5.—Patient No. VII, fourteen months after resection of two inches of the lower jaw for recurrent sarcoma attached to but not involving the bone.

Operation at New York Skin and Cancer Hospital November 6, 1913. Two curved incisions were made from the point of the chin to the angle of the jaw, enclosing a piece of skin measuring three inches by two inches. This skin with the tumor and two inches of the jaw bone were removed in one piece. The jaw was cut through just above the angle and just in front of the first molar tooth. The mucous membrane of the mouth was peeled from the jaw so that the mouth was not cut into, the only opening being where the single tooth remaining on the excised portion of the jaw, protruded through the mucous membrane. A part of the parotid gland and one inch of the internal jugular vein were also removed. The wound was entirely sutured with a small drain in the centre of it. The tumor was found to be a spindle-cell sarcoma.

The wound healed primarily excepting for a sinus in the centre, which persisted for two months. Nodules like enlarged glands gradually developed along the left sternomastoid, and a second operation for their removal was performed at New York Skin and Cancer Hospital, June 9, 1914. Through an incision from the left angle of the lower jaw nearly to the clavicle a chain of glands was removed. Some of these involved a part of the sternomastoid muscle, into which the tumor had spread. A portion of the muscle was removed, and the outer part of the sheath of the vessels for a considerable distance was also removed. As the spinal accessory nerve passed through the tumor a portion of it was removed. The glands on the right side of the neck, not having increased in size since the previous operation, were not dissected. Primary union resulted.

Pathological diagnosis by Dr. Jessup: recurrent sarcoma of the neck.

Nine months after this last operation there is no evidence of recurrence. Motions of the lower jaw from side to side, forward and backward, and upward and downward, are almost perfectly performed (Fig. 5).

Case VIII.—Male, aged fifty years. Following the extraction of a tooth from the left side of the lower jaw there was a persistent soreness of the gum and two months later a rapidly increasing swelling. Four months after the tooth was extracted the swelling was lanced externally. Blood and a little pus escaped and the opening never closed. Five months after the extraction of the tooth there were three openings in the left cheek, discharging pus and blood. The cheek and jaw were much swollen and the top of the gum from the angle of the jaw nearly to the median line was an ulcer with raised, irregular edges.

Operation at New York Skin and Cancer Hospital September 22, 1913. A portion of the left cheek measuring two by three inches, the left half of the lower jaw, excepting the upper part of the ascending ramus, and a mass of submaxillary glands, were removed.

The mucous membrane was entirely sutured and a flap of skin from the neck was swung upward to close the gap in the cheek.

Pathological diagnosis by Dr. Jessup: epithelioma of the jaw and masseter muscle, prickle-cell type.

Three months later the patient returned to the hospital on account of a recurrence just back of the chin and beneath the tongue. One-half inch more of the bone was removed together with a good deal of the floor of the mouth and the deeper tissues. Two weeks after this operation the patient had a sharp attack of dermatitis of the face and neck, probably an erysipelas.

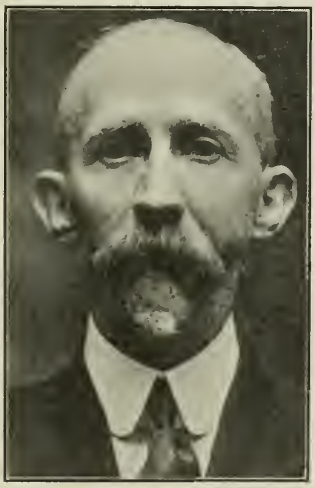


Fig. 6.—Patient No. VIII, sixteen months after resection for two inches of the horizontal ramus and one inch of the ascending ramus for epithelioma of the jaw and cheek. In two subsequent operations the left half of the bony chin and part of the lip, tongue, and floor of the mouth were removed. No apparent recurrence since the last operation, more than a year ago. Motions of the jaw are good, but the size of the mouth is much reduced by removal of one-half of the lower lip and a small part of the upper lip.

Three months after this second operation I again operated for a recurrence in the left side of the chin, extending through the floor of the mouth toward the base of the tongue. This was dissected out very much as one cuts the core from an apple. The tissue removed contained epithelioma.

Thirteen months after the last operation the patient was in good health and apparently free from recurrence, his wounds being entirely healed (Fig. 6).

Case IX.—Male, aged fifty-four years. Patient noticed a small "pimple" near the right lower wisdom tooth, for which in the succeeding two years he had two local operations and a cauterization. One pathological report was "non-malignant" and the other was "adamantinoma." The growth recurred in the site of the lower wisdom tooth with slight ulceration and the patient was unable to separate his front teeth more than one half an inch.

Operation at New York Skin and Cancer Hospital October 2, 1913. The tumor with a fair margin of sound tissues including the remains of the tonsil and parts of the pterygoid muscles were removed. The upper part of the jaw bone in the vicinity of the tumor was chiseled away. Dr. Jessup reported the tumor to be of epithelial type, probably malignant. The wound closed rapidly but did not entirely heal and the jaws gradually became more fixed so that they could scarcely be opened at all. A sinus persisted and granulations began to appear in it.

Operation at Miss Alston's Sanitarium April 23, 1914. A vertical incision from a point one inch in front of the ear was extended five inches downward into the neck. Branches of the external carotid artery and numerous veins were ligated. The parotid and submaxillary glands were dissected free and the inferior maxilla was cut through one inch in front of the ascending ramus. Its posterior portion was disarticulated and removed. Examination of the specimen showed that the lower jaw was hollowed out near its angle by a new growth which had deeply infiltrated in the region of the pterygoid muscles. The operation was difficult on account of the fixation of the jaw and the patient lost a good deal of blood. He recovered promptly and sat up in a chair for an hour on the third day. On the fourth day before leaving his bed he had an attack marked by pallor, weak pulse and respiration, without immediate loss of consciousness. Stimulants had no effect and patient died in about two hours, apparently from pulmonary embolism.

Case X.—Male, aged thirty years. A growth developed in the posterior part of the mucous membrane of the right cheek. At the end of three months it was ulcerating and measured about one and a half inches in diameter. The skin, tongue, and jaw bone were apparently not involved.

Operation at New York Skin and Cancer Hospital July 30, 1914. An incision was made from the angle of the mouth backward across the cheek. Skin flaps were dissected upward and downward and mucous membrane was incised one-fourth inch from the tumor, which was then dissected from the lower jaw and pterygoid muscles. The suture of skin was complete and that of the mucous membrane was carried out as far as possible.

Pathological diagnosis by Dr. Barber: epithelioma, prickle-cell type.

The wounds healed primarily but in three weeks there was an evident recurrence on the jaw bone and September 8, 1914, an incision was made from the angle of the mouth downward and outward to the angle of the jaw and then downward along the sternomastoid. A portion of skin overlying the tumor was excised, together with the submaxillary glands, a portion of the parotid, the jaw bone from back of the canine tooth to the middle of the ascending ramus, and a wide area of mucous membrane, all being removed in one piece.

Pathological diagnosis by Dr. Jessup: carcinoma of the lower jaw, involving the glands.

Wound healed primarily except at the drain site, but there was a rapid recurrence within the mouth in the site of the previous operation. The patient was so troubled with a foul discharge and a great deal of pain that six weeks later a large mass of tumor was cut out through the mouth and through the external wound. Relief was only temporary, and three weeks later a wider excision was practised, including the upper portion of the lower jaw and pterygoid muscles, both of which were badly infiltrated with the tumor. The pain and discharge were markedly relieved by the operation but in two weeks the space gained was again filling with tumor tissue, and the patient died six months after the resection.

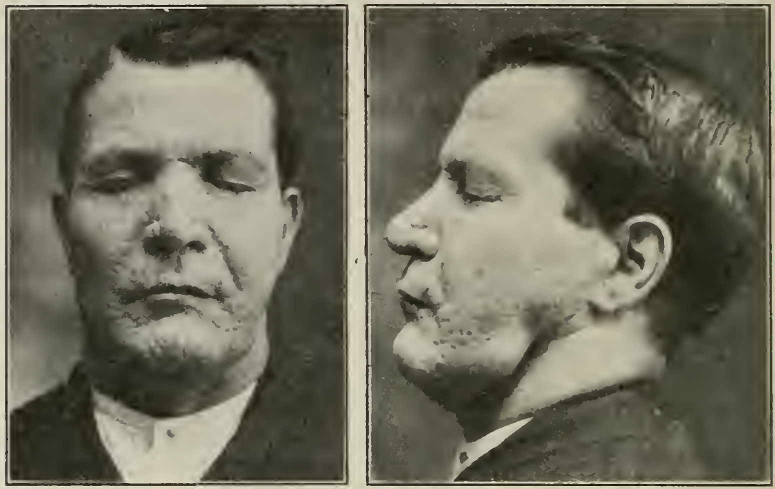
Case XI.—Male, aged fifty-four years. A growth in the region of the left tonsil, existing for a year, involved the tonsil, the anterior pillar, a part of the soft palate, and the mucous membrane between the upper and lower jaws and that of the lower jaw as far forward as the second molar, and the adjacent portion of the floor of the mouth and side of the tongue.

Operation at New York Skin and Cancer Hospital July 21, 1914. An incision starting one and a half inches from the chin was extended backward along the lower jaw to the angle and downward along the sternomastoid muscle. Skin flaps were dissected upward and downward. The parotid gland and facial nerve were exposed The dissection was continued across the cheek below these structures so as to save at least the upper branches of the facial. The jaw was cut through in front of the second molar and through the ascending ramus about one inch above the angle. An incision was made completely around the tumor in the mouth, and the whole mass of excised tissue was removed in one piece after division or the anterior branches of the external carotid and its terminal portions. The wound was partially sutured and drained.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type. Hyperplasia of nodes.

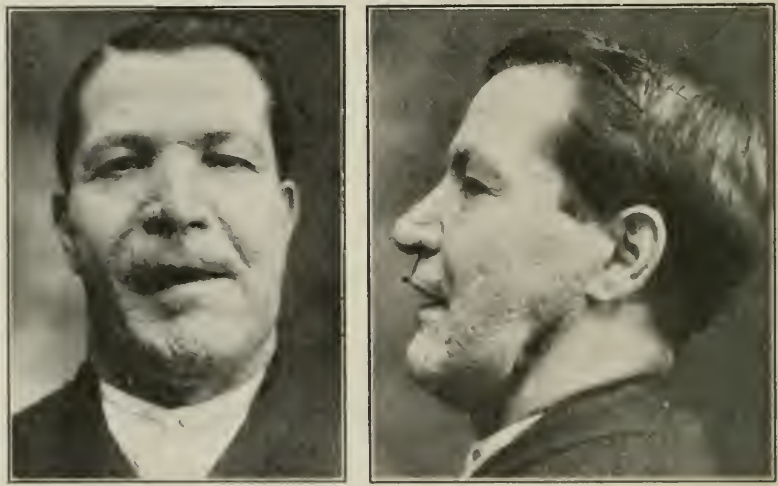
The patient had to be fed several days through a rubber tube, passed through his nose nearly to the stomach, as he could not swallow. His recovery was rather slow on account of difficulty in taking nourishment. Seven weeks after operation a piece of bone measuring one inch by one-half inch, dead and entirely loose, was pulled out through the mouth from the cut section of the ascending ramus.

Nine months after operation there was still a small sinus, but no evidence of recurrence (Fig. 7).



Front view, mouth and eyes closed.

Side view, mouth and eyes closed.



Front view, mouth and eyes open.

Side view, mouth and eyes open.

Fig. 7.—Patient No. XI, six months after resection of two inches of the horizontal ramus and one inch of the ascending ramus for epithelioma of jaw, tonsil, and adjacent parts. The whole pouch of mucous membrane between the cheek and tonsil, back of the jaws and which allows them to be separated, was excised. The resulting scar limits motion to an extent not seen after the usual resection; but the range of motion has increased since the photograph was taken.

Case XII.—Male, aged fifty-five years. The patient noticed a rough spot in the left cheek which gradually increased in prominence and later began to ulcerate. One year after it was first observed the growth measured three-quarters of an inch by one-half inch, being freely movable on the upper portion of the cheek, but glands were enlarged below the jaw.

Operation at New York Skin and Cancer Hospital November 13, 1913. A horizontal incision was made below the jaw and a second one from this upward across the cheek. The tumor with deeper tissues of the cheek down to the jaw bone, and a mass of fat and small hard glands from beneath the jaw were removed. The wound was sutured with drainage, and was slow in healing.

Pathologist reported the growth in the cheek to be a prickle-cell epithelioma, while the glands from the neck showed only hyperplasia.

In May, 1914, the patient went to another doctor, who removed a gland from above his clavicle under a local anesthetic.

In August, 1914, there was a recurrence in the posterior part of the alveolar process of the jaw and a hard area in front of the ear and another one above the left clavicle where the gland was removed.

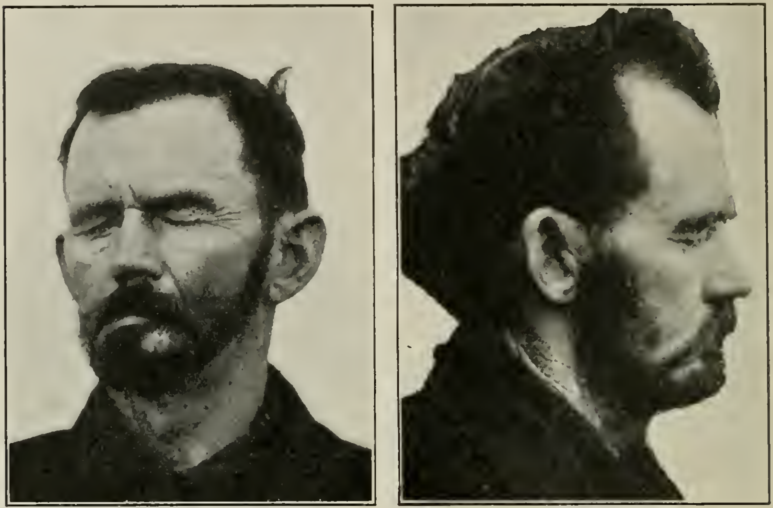
Second operation at New York Skin and Cancer Hospital, August 13, 1914. Incisions from the angle of the mouth were carried backward curving upward and downward so as to include a part of the cheek and neck. The jaw bone was cut through behind the canine tooth and in the middle of the ascending ramus. Several branches of the carotid were ligated. The mucous membrane of the cheek and floor of the mouth were cut through at a good distance from the tumor and the excised portion of the jaw with the tumor and glands attached to it were removed. The mucous membrane was sutured completely and the skin was sutured except for a distance of about an inch in the centre of the wound, where tension would have been too great.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type.

Recurrence rapidly developed and a palliative operation was performed September 10, 1914. Through a transverse incision beneath the chin a small mass of glands with the surrounding fat, fascia, and muscle were excised. The wound healed primarily, but additional points of growth showed themselves in the region of the tonsil, in the floor of the mouth, in the cheek, and also in the neck in front of the mastoid process.

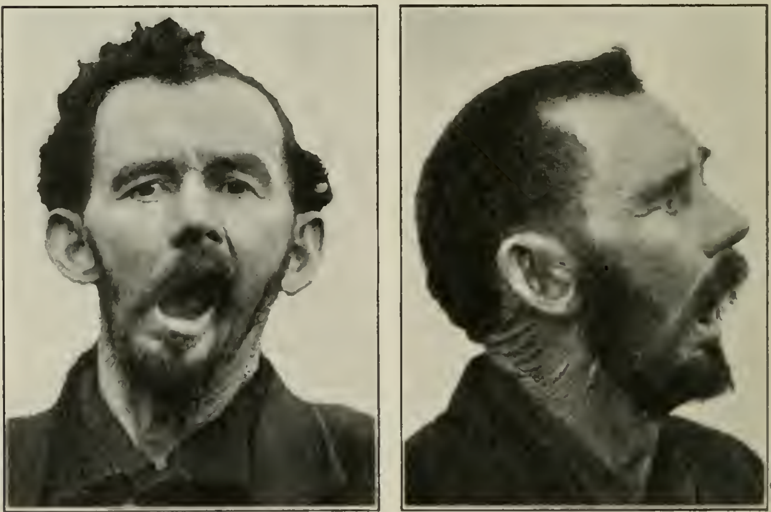
The patient died five months after the resection.

Case XIII.—Male, aged fifty-three years. The first symptom was a soreness of the inner side of the right cheek. Five months later a carious tooth and a portion of the right lower jaw were removed from within the mouth. Soon after this the cheek and jaw began to swell. Three months after this operation the mucous membrane covering the posterior half of the horizontal ramus, and a little of the ascending ramus of the right lower jaw, was the



Front view, mouth and eyes closed.

Side view, mouth and eyes closed.



Front view, mouth and eyes open.

Side view, mouth and eyes open.

FIG. 8.—Patient No. XIII, five months after removal of the right side of the lower jaw from the second bicuspid tooth to the articulation, for epithelioma of the cheek and jaw bone, involving the pterygoid muscles. Paralysis of the mouth and eye has diminished somewhat, and function is constantly improving, but lateral deviation is still marked.

seat of a leukoplakia, in the centre of which there was a papillomatous and ulcerating area. There were enlarged lymph glands in the region of the parotid, and about the bifurcation of the carotid. There was a small leukoplakia on the left lower jaw but no ulceration nor papilloma.

Operation at New York Skin and Cancer Hospital August 15, 1914. The skin was dissected back by an incision starting from the lobe of the ear, following the posterior and lower edges of the lower jaw to about the middle of the horizontal ramus and then curving downward to the centre of the sternomastoid. The neck was freely dissected from the hyoid bone to the ear. The branches of the external carotid and the internal jugular were divided. The parotid gland was removed from behind forward, the muscles of the jaw being cut just below the malar bone and dissected downward before the mouth was opened. The mucous membrane was then cut through wide of the involved area, the jaw sawed behind the second bicupsid, disarticulated, and removed with the attached portions of tumor and other soft tissues. Hemorrhage was profuse, and in spite of clamps and ligation the patient lost considerable blood, and the upper portion of the wound had finally to be packed with gauze. The mucous membrane of the mouth was easily sutured and the skin was sutured excepting for the drain site.

The patient made a good recovery, rapidly overcoming his operative anemia. The wounds where sutured healed primarily with very little leakage from the mouth.

Examination of the specimen showed the bone to be badly penetrated and there was excessive involvement of the pterygoid muscles.

Pathological diagnosis by Dr. Jessup: epithelioma, prickle-cell type. The enlarged lymph glands were hyperplastic only.

Eight months after resection the patient was in good condition. There was no sign of recurrence externally or internally. A minute sinus persisted at the upper end of the external scar in front of the ear, and there was a narrow streak of leukoplakia about one-third of an inch long in the mucous membrane just behind the point where the jaw was sawed through (Fig. 8).

Case XIV.—Male, aged forty-three years. A dentist called the patient's attention to a growth on the left lower jaw about the site of the bicuspid teeth. Three weeks afterward it was a tumor with a mushroom shape, measuring about three-quarters of an inch in diameter.

Operation at New York Skin and Cancer Hospital October 12, 1914. The growth was removed together with a narrow margin of healthy mucous membrane. The corresponding portion of the alveolar process was chiseled away.

Pathological diagnosis by Dr. Jessup: epulis, giant-cell sarcoma.

Six months later the patient was examined and there was no swelling of the jaw nor any other sign of recurrence.

SUMMARY OF CASES OF RESECTION OF LOWER JAW.

No.	Sex.	Age.	Physical examination.	Pathological diagnosis	Extent of resection.	Result.
I	M.	75	Jaw, ulcerating; recurrent after operation.	Epithelioma; bone involved.	2½ in. horizontal ramus.	Death in two months after operation elsewhere.
II	F.	45	Jaw, ulcerating; recurrent after operation.	Epulis; giant-cell sarcoma; bone not involved.	Alveolar process only.	Well; no recurrence for thirty-three months.
III	M.	44	Jaw, ulcerating; recurrent after operation.	Epithelioma; bone involved.	2¾ in. from chin backward.	Death in ten and a half months.
IV	M.	54	Mucous membrane of cheek.	Epithelioma; bone not involved.	From bicuspid teeth to joint.	Well; no recurrence for thirty-two months.
V	M.	34	Cheek; recurrent in jaw after three operations.	Epithelioma; bone involved.	From symphysis to above angle.	Death in nine months.
VI	M.	52	Jaw and glands; recurrent after operation in neck.	Epithelioma; bone involved.	From canine tooth to above angle.	Death in four months.
VII	M.	62	Neck below jaw; recurrent after operation.	Spindle-cell sarcoma; bone not involved.	From bicuspid teeth to above angle.	Operation after seven months for recurrence in neck; well; no recurrence for nine months since last operation.
VIII	M.	50	Jaw, ulcerating in mouth and through cheek; recurrent after operation.	Epithelioma; bone involved.	From near symphysis to above angle.	Two other operations for local recurrence in six months; well; no recurrence for thirteen months since last operation.
IX	M.	54	Jaw, ulcerating in mouth; recurrent after operation.	Carcinoma; bone involved.	From bicuspid teeth to joint.	Death in four days from embolism.
X	M.	30	Cheek, ulcerating in mouth; recurrent after operation.	Epithelioma; bone not involved.	From canine tooth to above angle.	Extensive local recurrence in spite of two more operations; death in six months after resection.
XI	M.	54	Cheek; gums; tonsil; tongue; soft palate.	Epithelioma.	From second molar to above angle.	Well; no recurrence for nine months.
XII	M.	55	Cheek and jaw, ulcerating; recurrent after two operations.	Epithelioma	Canine tooth to above angle.	Extensive local recurrence in spite of two more operations; death in five months after resection.
XIII	M.	53	Cheek and jaw, ulcerating in mouth; recurrent after operation.	Epithelioma; bone involved.	From bicuspid teeth to joint.	Well; no recurrence for eight months.
XIV	M.	43	Jaw in mouth.	Epulis; giant-cell sarcoma.	Alveolar process only.	Well; no recurrence for six months.

CERTAIN MEDICAL ASPECTS OF RECURRENT MALIGNANT TUMORS.

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It is frequently the experience of physicians to see a patient from whom a malignant growth has been removed long before, in whom recurrence has taken place, not at the site of operation, not in the shape of visible and palpable tumor masses in distant parts of the body, but with symptoms that resemble those of a so-called medical or internal disease as distinguished from the external or surgical, *i. e.*, operable affection. To such manifestation the term medical or non-surgical recurrence may be applied, though such a use of the term recurrence is open to criticism, because in the strict sense it is not a recurrence. The distant foci of tumor cells were already established at the time of operation, though dormant, but are now aroused into activity; or tumor cells slipped into the circulation during the manipulation of the operation and, lodging in distant parts, later as metastases, produce the symptoms to which reference has been made. So, also, these are really borderland cases and not strictly medical.

It is the purpose of this paper to call attention in a brief and practical manner to some of the very varied clinical manifestations of such recurrences as they might be met with in general practice. It is hoped that it may contain some helpful hints as to diagnosis.

Four things are likely to stand in the way of the early and easy recognition of the presence of these so-called medical recurrences: (1) The fact that there is no recidivation at the site of operation; (2) that no tumor mass can be made out in other parts of the body; (3) the long duration of time that may have elapsed since the operation, during which time the patient has apparently been healthy, and (4) the fact that the symptoms are not those commonly associated with tumor, but rather those of some other, often a so-called medical, condition.

The first three stumbling-blocks to diagnosis should be easily avoided by remembering that they are by no means exceptional, and should not be given much weight in excluding the presence of neoplasm. The thoroughness with which surgeons today remove tumors, *e. g.*, of the breast, makes recurrence *in situ* comparatively rare when an early diagnosis has made an early operation possible. A soft, pliable scar with no regional glandular involvement proves the concientious carefulness with which the surgeon has done his work, but does not exclude metastases elsewhere. And these metastases need not be large masses in order to produce symptoms. We are familiar with the large tumor in the abdomen that comes after the removal of a sarcomatous testicle; or the indurated mass found in the pelvis on rectal or vaginal examination, which represents the recurrence after the operation for carcinoma of the uterus or rectum; or the enlarged liver that appears after the removal of a melanotic sarcoma of the eye or a cancerous pylorus. But failure to find such frankly neoplastic deposits should not cause us to rule out the presence of smaller and hidden ones. Nor should a lapse of many months or even two or three years throw us off our guard and cause us to feel secure against return of malignant growth. Longer periods than this may elapse before there is evidence of metastatic activity. I have known eight years to pass after the removal of a carcinomatous breast before the patient succumbed to metastases which were evident only at autopsy.

The fourth difficulty is one not so easily surmounted. At times it is only by careful exclusion of other diseases, or by patiently tracing some atypical symptom or sign to its malignant source, that a correct diagnosis is made. And often this diagnosis can be only a presumptive one.

Some of these clinical features are worthy of special consideration. Among them are nervous symptoms, which may often accurately resemble those of other diseases. Thus pain in the lumbar, sacral, and gluteal region may readily pass for sciatica. It may, in fact, be genuinely sciatic in origin, a nodule pressing on this nerve or tumor cells invading the nerve sheath. At times, however, a careful examination will show a tenderness that is in the sacrum or the lumbar vertebræ, rather than in the nerve itself. It represents a bone metastasis, with perhaps pressure on the nerve roots as they leave the vertebral canal. One of the confusing features in some of these cases of severe lumbar and sciatic pains (and the same is true of Pott's disease and the spondylitis of typhoid) is the fact that the patients often become "nervous," sleepless, complaining, even hysterical, craving morphin, and the thought of the whole trouble being functional, a sort of railway-spine affair may be entertained. The true nature of the lesion may be revealed only when a pressure paraplegia supervenes. Neuralgic pains in other parts of the body, as in the intercostal nerves or in the scalp, may have their origin in deposits of tumor in bone. That certain tumors, as of the breast, thyroid, prostate, and adrenal, are prone to form metastatic deposits in bone is well known. No pain, therefore, occurring in a patient who has been operated upon for a malignant growth, and especially a growth in one of these organs, should be passed as due to simple neuralgia until careful search has been made to exclude bone metastases. At times an irregularity or swelling of the surface of the bone over the spot of tenderness will be helpful. The bone may crackle or fracture under even light pressure, as I have seen happen in the case of a rib. The roentgenogram may show focal changes in the bone and myelocytes or other blood change may be suggestive of involvement of the marrow in disease. A somewhat confusing feature is the disappearance of pain over the site of a bone deposit and the variation in tenderness that may materially change from day to day. Perhaps variation in circulatory conditions may explain these changes; and one may conceive of the tumor mass breaking through a surrounding shell of bone, the pain lessening as the pressure is relieved. Cerebral symptoms may be variable, *e. g.*, symptoms of brain tumor from metastatic deposits. In one case, months after an amputation of the breast, in which local recurrence had taken place, a sudden plugging of the central artery of the retina occurred, presumably by tumor cells.

Another group of symptoms, often confusing, concerns the respiratory tract. Long after the operation a patient may be taken with a cough, and then develop what seems to be an ordinary bronchial catarrh. The cough persists, dyspnea appears, and there is some cyanosis. The sputum is scanty, or it may be mucus or blood-tinged. Rales, dry and moist, may be heard in various parts of the chest, and possibly here and there is made out an area of harsher respiration, or perhaps a spot of dulness. There is little or no fever as a rule. Dyspnea may increase and the respiration grow hurried. There is some loss in weight. It is necessary for one to see an autopsy on only one of these cases, with the lung riddled with small or larger tumor nodules, to be able to understand how the condition resembles clinically miliary tuberculosis. Of course, larger masses may produce symptoms that are more clearly those of tumor. These larger tumors are more easily recognized, or at least suspected, from the predominance of pressure symptoms. The Roentgen rays in both types of thoracic metastases may be of material help in diagnosis.

Another metastatic phenomenon, often a late one, and often the first sign of failing health after the operation, is pleural effusion. Local pain with friction rub may clearly indicate involvement of the pleura; or dyspnea and dry cough may lead to an examination of the chest and a pleural cavity may be found to contain a large amount of fluid, no pain worthy of the patient's notice having been complained of. At times pain, some fever, or rapidly developing dyspnea will make the process resemble tuberculous pleurisy; or even a pneumonia may be thought of if bronchial breathing be detected in some part of the affected side. Rheumatic, tuberculous, and traumatic origin for the pleural fluid, as well as the ordinary causes for hydrothorax, must be excluded as accurately as possible. Bloody fluid obtained by exploratory puncture, the fluid perhaps containing tumor cells or large multinucleated cells, with mitotic figures, and lacking the lymphocytes and tubercle bacilli of tuberculous fluid, may be of material help. Often the fluid recurs even after repeated tappings that may be necessary for the relief of pressure. At times it will disappear. Such a disappearance took place in a remarkable case which I saw of late metastases months after the removal of a malignant syncytioma. Sudden large pleural effusion with pain and some fever followed the carriage into the pleura of the tumor cells. These apparently gravitated to the bottom of the pleura, where a large growth developed, invading the diaphragm and the lumbar vertebra, leading ultimately to paraplegia and death. No tumor mass was ever made out on physical examination during life, and no pelvic recurrence took place. The autopsy revealed the above chain of events.

Pleural fluid, therefore, in one who even years before has had a malignant tumor removed should arouse the suspicion of pleural metastases, nor should the temporary disappearance of this fluid lead to a too confident quieting of this suspicion.

Another remarkable phenomenon was seen in a young man of about twenty years, who consulted his physician for slight temperature, cough, and symptoms suggestive of incipient tuberculosis. A sudden and severe hemoptysis occurred. The acute anemia was extreme and out of all proportion to the amount of blood lost externally. Dyspnea was pronounced. The explanation was found in a hemopneumothorax. The lung had ruptured and a large amount of blood with air was in the pleural sac. Death from anemia seemed imminent, but after many days of delirium, prostration, and fever, due to the absorption of the blood, improvement occurred and the boy returned to his home. The explanation for this odd occurrence was found in a metastatic sarcoma of the lung. Five years before the boy's thigh was amputated for sarcoma of the tibia. No local recurrence. A few months after the pulmonary accident just described the boy died with every evidence of thoracic tumor. I have seen another case of metastasis in the pleura with fluid long after amputation of the leg for sarcoma, and one after removal of the testicle.

Just as a pleurisy, especially an afebrile pleurisy, should in these patients arouse a suspicion of the localization of secondary tumors in that tissue, so an otherwise unexplained ascites should lead to a careful examination for proof of the malignant origin of the abdominal fluid from direct involvement of the peritoneum or pressure on the larger trunks of the portal vein. Bloody or chylous fluid may be significant.

Personally, I have never seen clinical symptoms from involvement of the heart by tumor metastases following operation, though at autopsy symptomless nodules in the myocardium or pericardium are occasionally met with. Nor have I noticed clinically symptoms that could be referred to metastases in the kidney.

One type of disease due to these metastases is characterized chiefly by severe anemia and marasmus. This I have seen in a recurrence after removal of carcinoma of the breast. In this instance symptoms like diabetes insipidus were present for many weeks. While autopsy of the body showed numerous nodules, the brain was not examined. Perhaps here was the tumor that induced the polyuria, by pressure on the hypophysis. In another case a profound anemia much resembling pernicious anemia came on months after an operation for carcinoma of the penis.

Occasionally there is reluctance to accept a diagnosis of postoperative metastasis, because a nodule appearing after the operation in some distant part of the body has for a long time remained stationary in size, or has even at times seemed smaller. This should not, of course, rule out a malignant growth. The glands in the neck that are secondarily carcinomatous, as with primary cancer of the stomach, do not, of necessity, grow rapidly. I have seen a carcinomatous gland in the left side of the neck remain the size of a hickory-nut for a year, its first appearance being a few months after the removal of a breast for carcinoma. This patient had also carcinoma of the vertebra, with later paraplegia.

Every physician knows the danger there is in asking a patient what in the law courts are called leading questions. Unconsciously we may suggest answers to such a patient, or lead the history away from facts that would otherwise be clearly brought out by the patient's unguided recital of the history. But there are times when direct questioning is necessary and where it must be pressed. We know how a patient who fears tuberculosis will dodge and evade a direct answer that seems to him incriminating. One must often push the questions and insist upon definite answers.

Similarly, unless direct questioning is resorted to, one may sometimes fail to learn of the previous operation; the patient may forget to speak about it, or regard it as insignificant, or may be purposely concealing the fact. Even the physician may at times be inclined to underestimate the importance, from a diagnostic point of view, of the removal of a seemingly insignificant pigmented mole, or a "polypus" from the neck of the uterus. And the patient may have been given to understand that the tumor was innocent, though a telephone conversation with the surgeon who operated, or a reference to hospital records, might reveal the malignant character of the growth. A fear of learning the serious nature of the illness may induce a patient purposely to make false or misleading statements regarding previous operations, or to conceal the scars of these from the eye of the examining physician. I well remember a case of left-sided pleural effusion in a woman whose left breast had been removed some time before for carcinoma. The careful doctor had made several examinations of the chest, but through seeming modesty, as became a maiden lady of fifty, the clothing was on the occasion of these examinations always deftly arranged by the patient so that the scar of the operation was covered. Great was the surprise and embarrassment of the doctor as this scar came into view when, at the consultation, in response to insistent requests, the clothing was removed from the chest. The clue to the nature of the pleural effusion was evident. The possibility that a scar may mean the previous removal of a malignant growth should always be taken into consideration, whether such scar be on the lip, the scrotum, cervix uteri, the breast—in fact, anywhere. An absent eyeball has more than once led to the diagnosis of melanotic sarcoma of the liver.

In conclusion it may not be amiss, after having referred so often to the necessity of a thorough examination of these patients in whom there are obscure postoperative manifestations of malignant tumors, to call attention to the importance of such investigation before operation. A thorough exploration of the pelvis per vaginam and per rectum would sometimes ward off the useless operation for carcinoma of the stomach or breast. Secondary peritoneal tumors, as is well known, may sometimes plainly be made out on rectal examination. Such examination may readily be omitted when there are no pelvic symptoms, and when a palpable tumor of the stomach invites to operation. Unless obstructive or other urgent indications point to removal of the primary growth the detection of secondary deposits will contraindicate the operation. In three cases of hypernephroma I have seen operative removal of the kidney vetoed, once because of a secondary tumor in the brain, another time because of secondary deposits in the lung, and in a third case, the deciding voice being that of the late Christian Fenger, because edema of the leg made growth into the vena cava probable, and autopsy showed this to be the case. In a recent case secondary tumors in the lung decided against removal of a carcinomatous tongue. Percussion, auscultation, and the Roentgen rays all clearly showed the invasion of the chest. Such a warning as this may seem uncalled for. But clinical experience has made me feel that it may not be out of place to speak of these things, for it is often the well-known and commonplace that is forgotten, and that from time to time needs to be brought back to our attention.

VALUE OF RADIUM, SUPPLEMENTED BY CROSS-FIRE ROENTGEN RAYS, IN TREATMENT OF MALIGNANCY.[1]

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Much discussion has taken place in regard to the comparative value of radium, mesothorium, and the Roentgen rays in the treatment of malignancy, but in view of the present knowledge of radio-active substances and the Roentgen rays, it is impossible to advocate the extended use of one to the exclusion of the other. Each agent has its place. Both forms of radiation have wide ranges of usefulness which differ under certain conditions and in adaptability to parts affected. When the gamma rays of radium are filtered from the alpha and beta it is found that they conformed in most respects to that of the Roentgen rays. During the past few years physicists have proved that both the Roentgen rays and the gamma rays are ether impulses identical in nature, differing only in wave length and power of penetration.

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[1] Read before the Allegheny County Medical Society, January 19, 1915.

While today we are using Roentgen rays of much greater penetrating power and filtering out the lower inefficient rays, we must use different apparatus before we can produce rays with as great penetrating power as the highest gamma rays of radio-active substances. Many claim that the highest rays are unnecessary and have no therapeutic effect. This is a question still unsettled. Dessauer, of Frankfort, Germany, has constructed an apparatus which he claims produces rays which are, by every physical and biological test, identical with the gamma rays. He was to demonstrate this at the last meeting of the American Roentgen Ray Society in Cleveland, but, on account of the European War, was unable to be present.

The new tube invented by Coolidge, and used in many laboratories during the past year, marks a great advance because it provides much more uniform radiation which is essential in deep therapy. Coolidge is experimenting with a ray of much greater penetrating power than anything known except that produced by Dessauer, but has not placed this tube on the market. In a letter which I received from him recently he stated he would soon have this tube perfected by which any degree of penetration can be obtained.

With our present apparatus the therapeutic effects with the highest filtered Roentgen rays closely approach those of radium. There is no question that heavy doses of the filtered rays extending over not too long a period will cause the healing or disappearances of many malignant conditions which were unaffected by the inefficient treatment given a few years ago. After selecting the case, success or failure is rather a matter of technique, whether using radium or the Roentgen rays.

Both radium and the Roentgen rays as they are now understood have a different place in medicine and surgery than they had a few years ago. Those using radium had only small quantities, and often it was not of good quality, and the operators knew little or nothing about the necessity of filtering out the soft rays which did not penetrate, but which really predominated and acted as a caustic on the superficial tissues, nor did they understand much about secondary radiation. The same was true with those using the Roentgen rays. Any kind of a vacuum tube was used, no filters were employed, and usually the rays were directed in one direction toward the growth instead of using the present cross-firing methods, and with the tube placed at any distance regardless of the intensity without any instruments being used to measure the dosage.

There has been some rivalry between those using radium and the Roentgen rays, and as fast as one progressed the efforts of the other party to overtake its rival became more active. The inefficient Roentgen-ray work done in the early days and that which is being done at the present time by many accounts for some of the radium advocates making statements that there is no comparison in results between those produced by radium and the Roentgen rays. Many radium enthusiasts who are just beginning are making extravagant claims for radioactive substances because they have seen a few brilliant results for the first time, and they might be compared to the early Roentgen-ray extremists. Radium is an extremely valuable agent in the radiotherapeutic field, and extravagant and unwarranted claims will do much to hinder the avdancement of this branch of medicine. It can readily be seen that many physicians are judging both agents wrongly by the work being done by unqualified operators.

The experienced radiotherapeutists are the ones to whom we must still look for true information, rather than in books and the many periodicals lately published. The field of radiotherapy, meaning treatment by both radium and the Roentgen rays, is at present a kind of no one's ground and is suffering from incursions from every province of medicine and owning definite allegiance to none.

In treating a case either by radium, mesothorium, or the Roentgen rays we must always face a series of problems. Given a case with a certain lesion, its position, extent, its susceptibility to the influence to this or that radiation, when we must determine the agent or agents to use. The duration and method of application can be varied almost to infinity. This enables us to realize how rich radiotherapy should be in its results when properly selected and employed. In this connection let me quote several paragraphs from Dr. Francis Hernaman-Johnson in the October number of the *Archives of the Roentgen Ray:*

"It is, at any rate, certain that in cancer the therapeutic effects of hard filtered Roentgen rays closely approach those of radium. On the other hand, a wide gap yawns between the Roentgen-ray results of today and even those of a few years ago. A claim often set forth in papers and books on radium therapy is that rodent ulcers have been cured by radium after months of Roentgen-ray treatment had proved ineffective. My own experience would lead me to believe that sharp doses of filtered Roentgen rays extended over a period not exceeding one month will cause the healing of any rodent ulcer which is amenable to radioactive substance in any form. . . . The employment of rays which are too soft, or those of insufficient doses extending over a long period, does positive harm. If, however, the mischief is not too far advanced a few large applications of filtered Roentgen rays may cause healing, just as effectively as gamma rays."

In speaking of postoperative treatment Dr. Hernaman-Johnson describes the form of radiation in the following words: "An approximately uniform dosage throughout the whole of the suspected area is, therefore, the ideal to be aimed at. For the complete realization of this ideal two things are necessary: (1) rays so penetrating that they will pass right through the body with the loss of only a small fraction of their value, and (2) a parallel beam of such rays so that they shall not lose energy by spreading. Gamma rays fulfil the first condition. They will pass through 60 cm. of tissue before losing half their original intensity; but, to satisfy the second requirement, it would be necessary to suspend the tube some twenty inches from the skin, a procedure which would render useless even so large a quantity as 1000 mg. of radium salt. Hard Roentgen rays, on the other hand, though they fall to half value when they have penetrated about 10 cm. into the body, can be produced in any desired amount, so that what is to all intents and purposes a parallel beam may be played upon selected areas. Existing Roentgen therapy thus approaches much more nearly the requirements of prophylaxis than treatment by radium."

Then Dr. Hernaman-Johnson continues: "One of the great advantages claimed for radium over Roentgen therapy is that a tube of the radioactive substance may be buried within a cancerous tumor. In accordance with the law of inverse squares, the activity of such a tube diminishes rapidly toward the outer parts of the growth; so that the risk, on the one hand, of not killing outlying cancer cells, and, on the other, of seriously injuring healthy tissues, is one to be very carefully considered.

A study of the literature of radium therapy in cancer shows that both these happenings are not remote contingencies, but have actually, in numerous cases, been the cause of failure. If all tumors were perfect spheres it might be possible to calculate the exact quantity of radium required; but, unfortunately, cancer masses fail to conform to any of the figures with which we are familiar in text-books of plane and solid geometry. The recently introduced treatment by radioactive needles is open to the same objections, though in less degree. The only safe method, as in uterine cancer is to avoid huge doses, and to supplement the action of the radium tube by Roentgen-ray cross-fire outside."

Many observers who have used both agents extensively agree with Dr. Hernaman-Johnson, whose conclusions quoted are so clearly stated.

Every radiotherapeutist knows that the beam of rays given off from a Roentgen bulb or a radium tube is a mixture of heterogeneous rays, and that it is only by filtering and increasing the distance between the source of radiation that we can approach anything like a homogeneous ray. Then if we have homogeneous radiation we must not neglect the diminution of the distal dose by absorption by the tissues. There is always a difference between the proximal and distal dose. In using proper filtered radiation it has been estimated that each centimeter of tissue absorbs from 5 to 10 per cent. of radiation; so it can be readily seen that the deeper the growth is situated the more cross-firing with any form of radiation is necessary.

Dessauer considers that it would be necessary to have a radium tube containing 5 grams of radium when properly filtered and placed at the proper distance to give off a homogeneous ray equal to a bulb placed at the proper distance and properly filtered. No one has this amount or is it obtainable. This explains why most of the European workers who have had the best results in the treatment of malignancy long ago realized the importance of using the Roentgen rays from outside as an adjunct, and administering it through as many ports of entry as possible. In many places in the treatment of uterine cancer they used over forty ports of entry. This is a radical change from the technique that was used when the first cases of uterine cancer were treated by Roentgenotherapy years ago when little more than superficial or skin effect were produced. The treatment was given with an unshielded tube placed anteriorly to the abdomen the same as when making a radiogram.

It is generally accepted that equally good results can be secured by the use of radium or the Roentgen rays in the treatment of external epitheliomas, but, as a rule, most epitheliomas are treated by the Roentgen rays. It means nothing when some enthusiastic advocate of either the Roentgen rays or radium states that there is no doubt that one agent has been effective, whereas the other completely failed. Most likely the one applying the agent failed to recognize the limitations of his therapeutic agent, but when the epithelioma is situated on mucous membranes in cavities, radioactive substances will usually effect a cure unless too far advanced. Here radium always should have the preference. I believe no time should be lost in treating every case by radium as soon as diagnosed. The Roentgen rays should not be used through a speculum, thus losing valuable time if radium is available. I see so many patients coming late where the physician or surgeon had made an early diagnosis, and not knowing the value of radium, giving treatment by some other means when the lesion was situated so that it was inaccessible to any other form of treatment. Leukoplakia is a condition which can be cured by a few applications of radium or mesothorium and responds so unsatisfactory to any other therapeutic method. If left untreated the liability to ultimate malignant change must always be remembered. The stage at which an epithelioma situated on a mucous membrane is diagnosed and treated determines the prognosis more than any other malignant condition.

In carcinoma of the mouth, throat, rectum, or vagina the radioactive substance can be placed within the lumen of the organ or in close proximity to the growth, and, I believe, is superior to the Roentgen rays as far as the local treatment is concerned. But in all these cases—particularly if the disease is advanced and the lymphatics involved—the Roentgen rays are superior to any quantity of radium anyone has used up to the present time for the treatment of lymphatic glands. It must also be remembered that these high penetrating rays, given in great quantities and properly filtered, not only effect the adjacent lymphatic glands but also have a marked effect on the local tumor. In other words, it seems that the treatment is not complete if the radium is used locally unless it is followed for a certain length of time by Roentgenotherapy. Radium might be compared to surgery in its action on the local tumor. The great advantage of the combined treatment is thus self-evident. Some inoperable cases of carcinoma which have not been cured have been improved to such a degree that a subsequent operation could be performed. No matter how rare these cases may be, every case should at least have this amount of palliation. It is certainly true that the diagnosis of an inoperable malignant growth should not be equivalent to a death warrant to the patient. Postoperative treatment carried out in this manner would undoubtedly increase the number of permanent cures. If radiotherapy could change the percentage of cures in only a small percentage of the cases it is more than justified. It would seem that this is not advising too much when some noted German gynecologists advise radiation as the only method of treatment of operable cases of cancer.

Besides using radium in cavities I have been applying after operation a tube of radium in the axilla whenever it is possible, because it is often difficult or almost impossible in some cases for the patient to raise the arm sufficiently to give the desired amount of Roentgen treatment. Otherwise the results with modern Roentgen treatment are so good that, as far as external treatment is concerned, it seems radium has no advantage. When Roentgen rays are given prophylactically early, local recurrences are rarely seen. The great drawback is that the patients come to operation too late when deep metastasis has taken place. It is not enough in many cases to ray the axilla, the root of the neck, chest wall, and mediastinum, but the stomach and ovaries should receive attention. In order to have the best results the patients should not only come early but the lymphatics must receive radiation as uniformly as possible.

In an article on "Carcinosis of the Bone, Secondary to a Growth in some Epithelial Organ."[2] I mentioned the frequency of bone metastasis, and that it took place late, from three to five years after the cases were seen, and usually in the scirrhous type of carcinoma.

Limacher, who studied metastasis in mammary carcinoma, found the bones involved in about 14 per cent. of the cases. This shows the necessity of raying the cases thoroughly and early after operation, by the most efficient method possible.

In conclusion, the success of radium therapy in the treatment of malignancy is attained chiefly in those cases in which the radioactive substance is brought into contact with the growth, either in or on it, without an intervening layer of healthy tissue, and in which the thickness of the tumor does not exceed 4 cm. It is preferable to use the hard Roentgen rays for all deep-seated growths in which there is an intervening layer of healthy tissue. Radium gives the best results when it is brought in contact with the growth and supplemented by the Roentgen rays from outside by the cross-fire method. It is necessary for the operator to know the relative value of radium and the Roentgen rays when combining these two agents.

BLOOD TRANSFUSION: INDICATIONS; RESULTS; GENERAL MANAGEMENT.[1]

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and

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Blood transfusion, until recently, was expected to be a cure-all, and was tried in almost every kind of desperate condition. As the result of a large amount of work done since Crile's introduction of a successful technic for direct blood transfusion,[2] the real indications for transfusion have become better understood and more sharply defined. Crile's statement of the indications have, for the most part, remained valid, but subsequent experience has altered our views in regard to many of them. In particular the indications for transfusion have been extended by two facts: transfusion has become safe, and transfusion has become a much less serious procedure for both patient and donor. Clinical experience has shown that the tests for agglutination and hemolysis between blood of donor and of patient are reliable,[3] and except in the relatively uncommon emergency case in which there is not time to do these tests, we now approach a transfusion with absolutely no fear of this lurking danger. The danger of excessive transfusion (of which two instances occurred among the earlier of our cases) can be easily avoided—for direct transfusion by a simple method of calculation introduced by us,[4] and for indirect transfusion by accurate measurement of an amount of blood predetermined by such a calculation. The simplifications of technic, and especially the introduction of a good method of syringe transfusion by Lindeman,[5] have made transfusion a procedure which involves little trauma or pain, and which can be repeated on the same patient as often as desired. As a result of all this the tendency is more and more to use transfusion not as a means of last resort but as an ordinary therapeutic measure.

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[2] New York Med. Jour., December 2, 1911.

[1] Various parts of this paper were presented at a stated meeting of the New York Academy of Medicine, December 17, 1914, and at the meeting of the Association of American Physicians, May 11, 1915.

[2] Canada Lancet, 1906–07, xl, 1057; Ann. Surg., 1907, xlvi, 329.

In the present paper we have made a clinical study of 212 blood transfusions in 189 cases which we have had the opportunity of observing either in the hospital or in private practice. These transfusions were done by a number of different surgeons, and for a great variety of different conditions.[6] In many of the cases the indications had been established by previous work: on the other hand some of the transfusions were practically experimental. Of these, some were successful and others, in the light of the experience thus gained were cases in which even under the best possible conditions little or nothing can be expected from transfusion.

We shall refer only incidentally to the now rapidly growing literature, as we believe that more will be gained by presenting our own conclusions fully and leaving it to the reader to compare them with those of others.

We shall first briefly summarize the general results of all the transfusions (Part I) and shall then discuss in detail the results in each of the conditions for which transfusion was done (Part II); and finally (Part III) we shall discuss certain details concerning the general management of transfusions.

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[3] Ottenberg and Kaliski, Jour. Amer. Med. Assoc., 1913, lxi, 2138.

[4] Libman and Ottenberg, Jour. Amer. Med. Assoc., 1914, lxx, 764.

[5] Amer. Jour. Dis. Child., 1913, vi, 28; New York Med. Rec., 1912, lxxxi, 979.

[6] We wish to thank the members of the Attending Staff of the Hospital for their generosity in permitting us to utilize the records of the cases that we studied in their services. We are also under obligations to many physicians whose private cases we followed with them.

Part I.

GENERAL SUMMARY OF RESULTS.

One occasionally hears the opinion put forward that transfusion after all has not turned out to be a useful procedure, that there are few cases in which it really does good, and that it will probably be dropped again just as it was thirty years ago after the wave of enthusiasm for it following the Franco-Prussian War. For this reason we present the following general summary of the successes and failures in the 189 cases which we have seen. The proportion of successful results in the future will undoubtedly be far greater than in the past, not only because of recent technical improvements but because the indications will be more definitely known and the discrediting transfusions in hopeless cases, in which transfusions can not possibly be of avail, will not occur. The cases are subdivided according to the following scheme:

I. Successful cases.
  1. Cases in which the prognosis was extremely bad, and transfusion saved life.
    (*a*) Cases which subsequently completely recovered.
    (*b*) Cases in which the original underlying disease continued.
  2. Cases which recovered but in which the prognosis before transfusion was not desperate.
II. Unsuccessful cases.
  1. Cases in which there was temporary improvement following transfusion, with death later from continuation of the original disease.
  2. Cases which died of some disease necessarily fatal and in which transfusion could not have been expected to do much good.
  3. Cases in which transfusion did little or no good, although from the nature of the disease a good result might have been possible.

I. Successful Cases. 1. *Cases in Which Transfusion Saved Life.* There are 42 cases of this kind—that is to say, cases which almost undoubtedly would have died in a short time if transfusion had not been done. Of these, 29 subsequently recovered entirely and were discharged well or have continued under observation up to the present time; 13 were saved from immediate death but have continued to suffer from some chronic condition which could not have been cured by transfusion (pernicious anemia, leukemia, etc.).

(*a*) *Cases Which Ultimately Recovered.* Almost all the 29 cases which were rescued from immediate death were cases of hemorrhage. There were 9 cases of gastric or duodenal ulcer with extreme hemorrhage; 3 cases of hereditary hemophilia; 3 cases of ectopic pregnancy; 7 cases of hemorrhagic diathesis; 1 case of sloughing uterine fibroid with hemorrhage; 1 case of cholemic hemorrhage; 1 case of hemorrhage after a kidney operation; 1 case of illuminating gas and morphine poisoning; 1 case of typhoid hemorrhage.

(*b*) *Cases in Which Life was Saved by Transfusion, but in Which the Underlying Disease Continued, or Which Ultimately Left the Hospital in Greatly Improved Condition or Are Still under Observation.* These 13 cases include 6 patients with pernicious anemia who lived for long periods after apparently life-saving transfusions; 2 cases of cancer in which persistent hemorrhages stopped; 1 case of hemorrhagic diathesis with grave anemia, who left the hospital in improved condition against advice; 1 patient with a tumor of the spleen and grave anemia of unknown origin and 1 case of chronic leukemia.

The cases, then, in which transfusion was apparently life-saving fall under four main headings:

Acute anemia from hemorrhage.
Hemorrhagic diathesis, whether hereditary or acquired.
Grave chronic anemias.
Poisoning.

2. *Cases Cured or Greatly Benefited, Not in Desperate Condition at Time of Transfusion.* There were 43 cases in which transfusion was not an emergency measure but was performed on patients whose general condition had been seriously impaired by chronic disease. Most of these patients ultimately made complete recoveries, others continued to suffer from the chronic illness. In all the cases there was great improvement following the transfusion.

There were among these, 3 cases of gastric or duodenal ulcer which had repeated hemorrhages but were not in desperate condition at the time of transfusion. Undoubtedly recovery in these cases was greatly hastened by transfusion. The same may be said of 2 cases of dysentery with marked anemia. In this group also were 9 cases of pernicious anemia with marked remissions; 3 of the cases were instances of severe infection from osteomyelitis, in which the increased strength given by transfusion undoubtedly brought about the ultimate recovery; 9 were cases of malignant disease which were greatly benefited by the transfusion, 3 of them undergoing subsequent radical operations.

Of the 189 transfusion cases, then, 85 (or 45 per cent.) were successful in that the condition of the patient was greatly improved, and 42 of these (or 22 per cent. of the whole number) were life-saving.

II. UNSUCCESSFUL CASES. There were altogether 104 cases in which transfusion did no good or in which the continuation of the original disease caused death. (This is exclusive of a few early cases, not enumerated in the present series, in which the operation of transfusion itself was not successful, *i. e.*, no blood, or very little passed from donor to patient.)

1. There is a first group of 28 cases which improved for a short time but died subsequently from continuation of the original disease. These included a considerable variety of diseases, chief among which were malignant tumors, pernicious anemia, subacute streptococcus endocarditis, dysentery, typhoid fever, and pyogenic infections. These were all cases which lived from several days to one and a half years after transfusion.

2. The second group of the cases which died consisted of 23 cases of some disease of itself so grave that transfusion could not have been expected to do much good, and was only resorted to as a desperate hope. These included cases of acute lymphatic leukemia (3 cases), typhoid perforation (1 case), brain tumor (1 case), diabetic coma (3 cases), uremia (1 case), hemorrhagic diphtheria (1 case).

3. The third group of fatal cases consisted of 23 patients in whom transfusion might have been expected to be beneficial, but actually did little or no good. Of these the most disappointing were 4 cases of postoperative shock and 6 cases of pathological hemorrhage (including 4 of cholemia and 2 of purpura hemorrhagica). In these instances, contrary to expectation, the hemorrhages were not influenced by transfusion. There were also 3 cases of hemorrhage in typhoid fever.

Finally, there were 2 cases (1 of pernicious anemia and 1 of subacute streptococcus endocarditis) in which the unfavorable outcome was hastened by transfusion of excessive amounts of blood and 3 cases in which the fatal result was probably due to transfusion of incompatible (agglutinative and hemolytic) blood.

Part II.

SPECIAL INDICATIONS.

These are subdivided according to the following scheme:

I. Transfusions for simple hemorrhage.
    1. Gastric and duodenal ulcer.
    2. Dysentery.
    3. Typhoid hemorrhage.
    4. Ectopic pregnancy.

II. Transfusions in connection with surgical operations.
    1. Preliminary to operation.
    2. For postoperative hemorrhage.
    3. For shock.

III. Transfusions for the cure of hemorrhagic conditions.
  1. Purpura hemorrhagica.
  2. Hemophilia.
  3. Hemorrhages secondary to
    (*a*) Blood diseases.
    (*b*) Severe infections.
    (*c*) Jaundice (cholemia).

IV. Transfusions for blood diseases.
  1. Pernicious anemia.
  2. Leukemia.

V. Transfusion for infections.
  1. Infections with pyogenic organisms.
  2. Subacute streptococcus endocarditis.

VI. Transfusions for intoxications.
  1. Acute poisoning.
  2. Diabetic coma.

VII. Transfusions for debilitated conditions.
  1. Cancer.
  2. Malnutrition.
  3. Simple anemia.

I. TRANSFUSIONS FOR SIMPLE HEMORRHAGE. 1. *Gastric and Duodenal Ulcer.* There were altogether 14 cases of gastric or duodenal ulcer transfused. Almost all of these were in desperate condition at the time the transfusion was done; 12 of the 14 recovered. The 2 deaths occurred not from a continuance of the hemorrhage but from peritonitis and other complications following the laparotomy. Of the 12 cases which recovered, 4 were cases of duodenal and 8 of gastric ulcer. In all the cases there was a severe anemia, and actual hemorrhage was still going on at the time of the transfusion.

The hemorrhage in these cases was slight at the time, probably due to exsanguination, and the transfusion seemed to exert a beneficial effect on the hemorrhage itself.

Of the 2 cases which died, 1 was a case of duodenal ulcer, 1 a case of multiple gastric ulcers complicated by a cholecystitis; 1 of these cases continued to bleed after the transfusion. Death in this case was not due to the bleeding, however, which was relatively slight, but to a general peritonitis following pylorectomy.

The results in the gastric and duodenal ulcers show that transfusion exerts an exceedingly favorable effect on hemorrhage. It should be said that the two fatalities in ulcer cases were among the three operated cases, but that in these three cases the operation had to be performed for other indications than hemorrhage.

There were 4 additional cases of severe gastro-intestinal hemorrhage not included in the list of gastric ulcers. Only 1 of these recovered. One was a patient who had been suffering from a chronic anemia with a large spleen for a year or more, and who suddenly had a profuse gastric hemorrhage. A large transfusion was done, but the hemorrhage continued and the patient died within twelve hours. It seems likely that the hemorrhage may have been due to thrombosis of the splenic vein. Another was a case of profuse gastric hemorrhage secondary to cirrhosis of the liver; this case recovered. The third was a fatal case of postoperative gastric hemorrhage following extirpation of the rectum for carcinoma; and the fourth, a case of hemorrhage from a carcinoma of the stomach in which the patient died after a subsequent operation.

It is a striking fact that in almost all the cases of gastric or duodenal ulcer the hemorrhages stopped after transfusion. At first there was considerable hesitation about transfusing these cases during active hemorrhage on account of the danger of raising the blood-pressure and thus increasing the hemorrhage. This danger undoubtedly does exist, and because of it we would warn against transfusion in acute first hemorrhages (except for the purpose of saving the patient from immediate exsanguination).[7] *The cases in which transfusion seems actually to check hemorrhage are those of repeated or prolonged bleeding.* In these cases (as anyone who has tested the coagulation time of many patients has observed) the coagulation time of the blood is normal or even shortened, but the clots are of a flabby nature, different from the firm tough clots of chronic anemias. It seems likely that these soft clots form imperfect thrombi and thus the mere prolongation of a hemorrhage causes a vicious circle and tends toward its further prolongation. Transfusion checks the hemorrhage by supplying blood which can form normal thrombi.

The same explanation of the hemorrhage-checking effect of transfusion applies, of course, not only to gastro-intestinal, but to other forms of prolonged hemorrhage, and partly to the hemorrhagic diatheses.

2. *Dysentery.* There were transfusions in 6 cases of severe dysentery. These patients were all profoundly anemic, due not only to hemorrhage, but to nutritional disturbance. In all the cases the immediate results of the transfusions were very good, but in 4 of the 6, the intestinal disturbance continued and the patients ultimately died. In one of the patients the dysentery finally yielded to treatment and recovery ensued. In 1 the general condition was bettered, but the patient has continued to suffer from intestinal symptoms.

In severe dysentery, then, transfusion is worth trying as a temporizing measure.

3. *Typhoid Fever.* As the chief indication for transfusion in typhoid fever is usually hemorrhage, all the cases of typhoid fever

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[7] Repeated small transfusions done by the newer methods would, however, be applicable (see Addendum).

will be summarized here. There were nine transfusions in 7 cases of typhoid fever. Of the 7 patients, all in the most desperate possible condition, 2 ultimately recovered. One of the fatal cases should perhaps be excluded, as it was a case of intestinal perforation in which transfusion was done in the hope of bringing the patient, already in profound shock, into a condition in which an operation could be done. The transfusion was without effect. The 6 other patients suffered from severe and protracted hemorrhage. In the 2 who recovered the hemorrhage practically ceased after the transfusion. Of the 4 who died, 3 had hemorrhages so large that transfusion could accomplish nothing. In the fourth the hemorrhages stopped for a time after transfusion only to begin again after a few days. Two weeks later a second transfusion again relieved the symptoms due to hemorrhage, and the bleeding stopped. The fever continued and the patient died three weeks later of exhaustion. If, as seems fair, we include the two transfusions in this case among those in which the symptoms of hemorrhage were relieved by transfusion, we can say that there were four such transfusions among the seven done for typhoid hemorrhage.

One of the 2 cases that recovered has been reported by Dr. Manges,[8] with whom we had the privilege of observing the patient. In this case two transfusions were done. After the first the hemorrhage ceased. There continued, however, a remarkably protracted and severe typhoid infection, and there developed a general streptococcus infection. A second transfusion was done a month after the first, and the patient recovered with surprising promptness.

As the two patients who recovered would in all probability have died without transfusion, it is undoubtedly a useful method in the treatment of severe typhoid fever. In the presence of exceedingly large hemorrhages it can have, of course, only a temporary stimulating value. In cases of protracted or repeated hemorrhage it not only replaces the lost blood, but may help check hemorrhage. (See above under Gastric Ulcer.) *In all typhoid cases the first appearance of blood in the stools should be an indication to make preparations so that a transfusion can be done, if needed, at very short notice.* If the transfusion is not needed, little is lost; if it is needed, invaluable time is gained. Finally, in the typhoid state and in very protracted cases of typhoid, transfusion may have life-saving value and should be tried oftener than it has been.

4. *Ectopic Pregnancy.* There is perhaps no single condition to which transfusion would seem to be more ideally suited than ruptured ectopic pregnancy. There were three such cases in our series, and in all of them the transfusion was life-saving. The circumstances of the transfusion in the three cases differed slightly.

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[8] New York Med. Rec., 1912, lxxxi, 979.

The one was an emergency case, an almost exsanguinated patient, and a transfusion was done immediately after the operation. Another had been operated upon, but two days after the operation she was doing badly and a large transfusion was done. The third was a case which bled slowly and in which the diagnosis was at first not certain. A transfusion raised the hemoglobin from 25 to 50 per cent., and a successful laparotomy was performed two days later.

II. Transfusions in Connection with Surgical Operations. 1. *Preliminary to Operation.* Among the most satisfactory transfusions in the whole series were some of those done preliminary to an operation upon patients whose desperate condition would otherwise have contra-indicated any operation. There were 33 such preoperative transfusions and in 13 of them the result was decisive and the patients recovered. The actual effects of such transfusions are even better than these figures show, because a majority among those that died did so as a result of postoperative complications (such as peritonitis or pneumonia) or of a continuation of the original disease (such as metastatic carcinoma). Three died of operative shock; and our experiences have not led us to think that transfusion has any specific effect in preventing shock further than its effect in restoring to the patient more or less of his original power of resistance.

2. *For Postoperative Hemorrhage.* Little need be said about postoperative hemorrhage that has not been said about hemorrhage in general. Transfusion is the ideal remedy, but, of course, if the hemorrhage is not at the same time checked the ultimate outcome will not be affected. There were 5 transfusions for hemorrhage after operation (not including the transfusions for postoperative hemorrhage due to cholemia, which will be discussed separately). In 3 of the cases there were brilliant recoveries, in 2 death. In the 2 fatal cases (nephrotomy and operation for malunion of fractured femur) shock probably played almost as large a role as hemorrhage. (In the former of them transfusion of incompatible blood may have been a contributing factor.[9])

3. *For Shock.* There were seven transfusions for postoperative shock. All the patients died within an hour to five days, and it seems probable that transfusion is not to be relied upon clinically as a remedy for pure shock. In four of the cases (nephrectomy, bone-plating, prostatectomy, amputation of leg) hemorrhage played an important but secondary role. The results are the more disappointing as shock is one of the conditions in which it was at first thought, from the experimental work of Crile and his collaborators, that transfusion would be life-saving. This much, however, is to be said about our results: the transfusions were all done late,

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[9] See below under Dangers of Transfusion.

after the shock had lasted for some hours to several days. It is possible that if the condition of shock could have been foreseen and transfusion done immediately after the operation instead of after many hours of delay the results (especially in those cases combined with hemorrhage) might have been better.

III. Transfusions for the Cure of Hemorrhagic Conditions. The group of hemorrhagic diseases is a heterogeneous one comprising a number of conditions of very diverse pathogenesis. For practical purposes the 35 cases in our series can be grouped under (1) idiopathic purpura hemorrhagica, (2) hemophilia, and (3) secondary hemorrhagic disease complicating such conditions as severe infections, pernicious anemia, leukemia, and prolonged jaundice. Of hemorrhagic disease of the newborn, which has proved so brilliant a field for transfusion therapy, there was only one case in our series, and as the disease in this case was probably secondary to a staphylococcus infection, it will be included under the heading of secondary hemorrhagic disease.

1. *Purpura Hemorrhagica.* Idiopathic purpura hemorrhagica is characterized by the occurrence of spontaneous hemorrhages in various locations. The number of blood platelets is usually decreased greatly, but the coagulation of the blood is generally unimpaired. These two laboratory criteria were sought for and found in most of the cases of our series. The milder purpuras, as a rule, recover spontaneously. The more severe ones are frequently fatal, and it is only in this class of severe purpuras that transfusion is often used.

There were twelve transfusions in 9 such cases of severe purpura. Of the 9 cases, 2 died, uninfluenced except as to temporary replenishment of blood, 6 recovered completely, and 1 left the hospital improved. More striking than the statistics (especially in a disease of which the milder cases usually recover) was the prompt cessation of hemorrhages in most of the cases. This phenomenon leaves little doubt that beside the effect of transfusion in replacing lost blood, it has a definite curative value in these cases. On what the curative value depends is at present not at all clear. It is evidently not due to restored coagulability of blood (as it is in hemophilia), for in purpura the blood clots normally. That it has some connection with the fresh supply of blood platelets seems likely. Platelets have been shown to possess an important function in thrombus formation quite apart from their role in mere blood coagulation. But the normal life duration of platelets is known to be very short, and it does not seem probable that the relatively limited supply of platelets, even in a large transfusion, can account for all the benefit produced.

Of the 9 cases, the 2 which were fatal form a peculiar group, because they were both cases of postpartum purpura hemorrhagica. In both cases the hemorrhages were entirely uninfluenced by rather large transfusions. It is possible that the pathogenesis of these cases is different from that of the others.

Of the 7 cases which recovered all were in desperate condition at the time of transfusion, in 6 of them the hemoglobin being reduced to between 10 and 25 per cent., and in the seventh, to 42 per cent. In 4 of these cases the cessation of hemorrhages was prompt and complete after transfusion. (In 1, however, a case with ecchymoses, hemorrhages from the gums and profuse uterine hemorrhage, the uterine hemorrhage recurred after four months. A hysterectomy was done and the patient recovered, and according to the notes supplied us by Dr. Maybaum the patient has remained well for seven months.) In the other 3 cases the cessation of hemorrhage after transfusion was not complete; slight subsequent hemorrhages did occur, but the turn for the better was unmistakable; 2 of them ultimately recovered completely; the third, in spite of three transfusions, was still suffering from purpura when she left the hospital after three months.

In all of these cases, before transfusion was resorted to, attempts were made to check hemorrhage by serum treatment—subcutaneous, intravenous, or local use of human, horse, or rabbit serum—and entirely without effect. We will return to the subject of serum treatment under the heading of hemophilia.

2. *Hemophilia.* This disease is one in which transfusion may fairly be spoken of as specific therapy for the control of hemorrhages. The exact pathogenesis of the hemorrhages is not entirely understood, but what we do know throws considerable light on the mode of action of the transfused blood. When blood is obtained from the vein of a hemophiliac during an interval between hemorrhages, the coagulation time is enormously prolonged but the clot which finally forms is normal in texture and amount. Analysis shows that the delayed coagulation is due to deficiency in some element that goes to form thrombin (fibrin ferment). Experimenters are not all agreed as to which element is lacking, but the preponderance of evidence favors the view that the power of producing the activating substance (known under a variety of names—thrombokinase, thromboplastin, cytozyme) is diminished in the circulating blood. On the other hand (and this is a very striking fact) there is evidence that this activating substance is not lacking in the tissue cells. And this corresponds to the well-known clinical fact (confirmed by us in a number of cases) that in hemophilia, even when blood obtained directly by venipuncture shows greatly prolonged coagulation time, blood obtained from small cuts or pricks, clots in approximately normal time. It is clear that transfusion stops hemorrhage in hemophilia by supplying the patient's blood with the lacking element; and it is also clear (*a priori* as well as from our clinical experience) that such cures are not permanent, that sooner or later the fresh supply of thrombin-forming substance

must become exhausted and the tendency to hemorrhage exist anew.

There were five hemophilia cases in our series. All were males; four were children. Three gave typical family histories. The fifth case was a boy of sixteen and no family history of bleeding could be obtained, but the hemophilia had existed from birth.

The first case was not anemic but had a history of repeated hemorrhages from various sources, and was admitted to the hospital with hemorrhages into several joints. After the transfusion there were no further hemorrhages, and the patient left the hospital in good condition. He reëntered the hospital three months later with renewed hemorrhages into the joints and from a small wound. The second case was a brilliant cure, the child being almost completely exsanguinated before the transfusion. No further hemorrhages occurred after the transfusion. In the third case, in spite of a successful transfusion, bleeding from a small wound in the chin stopped for only twenty-four hours after transfusion. The patient was taken home against advice and lost track of. The fourth case was a child with protracted hemorrhage from a cut in the mouth. Bleeding stopped at once after an intravenous injection of 25 c.c. of whole blood from the father. The fifth case was a boy aged sixteen years, who had since birth had repeated hemorrhages from various parts of the body, and who twice underwent probably life-saving transfusions when almost exsanguinated. In each instance hemorrhage stopped at once after transfusion.

Including the two transfusions in the fifth case, we can then report six transfusions in hemophilia cases. In all but 1 of the cases the transfusion was only done after protracted hemorrhage had failed to yield to all other kinds of treatment, including serum treatment. In five out of the six transfusions the hemorrhage was checked promptly and the patients regained good health. In the 2 cases that could be followed for some time the tendency to hemorrhage reappeared after weeks or months.

Hemophilia is a disease with a high mortality. The majority of persons afflicted with it never reach adult life. (This is what has given rise to the erroneous statement that the disease is only transmitted by females.) Transfusion, it seems to us, offers a new hope for these doomed individuals, and we would suggest the following plan of procedure:

Every individual known to have hemophilia ought to have at his command several persons whose blood by previous tests[10] *is*

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[10] Such tests, once performed, would not need to be repeated when the transfusion is done, since the agglutinative property of the blood of certain individuals for the blood cells of certain others are permanent for life, and the hemolytic property which occasionally occurs develops, as a rule, only where there is already agglutinative power present. However, if transfusions are repeated the tests should be repeated also. as we know from experimental work (Ottenberg, Kaliski, and Friedman, loc. cit.) that it is possible to develop immune isohemolysins by repeated direct transfusions.

known to be compatible with his, and who are willing, when called upon, to give blood for transfusion. These donors, if relatives of the patient, should have the possible existence of latent hemophilia excluded by blood tests as well as by consideration of the hereditary laws of the disease. Whenever serious hemorrhages occur, prompt transfusion should be done, preferably by the syringe method, as this does not injure the vein, and hence allows for any number of future transfusions. It seems to us possible that by this system the majority of hemophiliacs might be enabled to lead a life of normal duration.

It seems to us, further, that in these cases the prophylactic effect of small transfusions (25 to 50 c.c.) repeated at long intervals (one to three months) would be well worth trying. Such injections of one or two syringefuls of unaltered blood could easily be performed as an office procedure by any one skilled in the syringe method.

Comparison of Transfusion with Serum Treatment. Almost all the hemorrhagic cases (including those to be described below) and a number of the cases of hemorrhage from other causes (such as typhoid ulceration and gastric ulcer) received subcutaneous or intravenous injections of fresh serum before transfusion was resorted to. Without going into details we believe we can say that the serum treatment was given a fair trial; the serum was used in large amounts and repeatedly. We have also had a considerable experience with serum treatment in cases which did not come to transfusion. In spite of the occasional cessation of hemorrhages after such serum injections we have not been able to convince ourselves that serum injections have any effect on hemorrhage. In 2 hemophilia cases (not transfused) the coagulation time was no shorter after than before serum injections (subcutaneous in one case, intravenous in the other).[11] On the other hand, we have often seen serum or defibrinated normal blood show an unmistakable effect in stopping hemorrhage when applied directly to small bleeding points.

The rationale of serum treatment and of transfusion for hemorrhagic conditions is indeed different. The active ingredient of serum is thrombin (fibrin ferment). Thrombin never exists in circulating blood but is formed only when blood is shed. When injected into the circulation it is at once neutralized by the antithrombin which exists in blood plasma. If it were not so neutralized it would cause intravascular clotting. Serum, therefore, cannot be expected to exert any thrombin action at a bleeding point distant from the point of injection. Whatever distant effect it has is probably in the easily assimilable nutrition which it offers, or possibly the serum ingredients can be made over by the body into the predecessors of thrombin. Transfusion of whole blood, on the other hand, supplies the body at once with all the substances in plasma, cells and platelets necessary to elaborate thrombin at a distant bleeding point.

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[11] It is of interest to note that we once saw bleeding stop (case of carcinoma of pancreas, icterus, general hemorrhages) following the use of serum, although the coagulation time became much longer. The coagulation time is not, therefore, always an index of the bleeding tendency.

Nevertheless, on account of the favorable reports of others, and particularly on account of the successes reported in hemorrhagic disease of the newborn (a condition with which we have had little experience), we believe that serum treatment deserves a further clinical trial.

2. *Secondary* (*symptomatic*) *Hemorrhagic Disease.* Hemorrhagic disease is frequently secondary to some other condition, such as severe infectious diseases, blood diseases (leukemia, pernicious anemia), and intoxications (nephritis, jaundice, etc.). It seems probable too that further study will show that many of the cases now classed as idiopathic are really secondary. There were 18 undoubtedly symptomatic cases in our series, 3 secondary to infections, 5 to leukemia, 1 to pernicious anemia, 8 to cholemia (prolonged jaundice), 1 to nephritis.

The pathogenesis of the hemorrhages in these secondary cases is variable, as Whipple and others have shown. In some, deficiency in fibrinogen, in others a lack of some of the ferment-forming substances, and in still others an excess of antithrombin have been demonstrated. Whatever the pathogenesis, however, the transfusion of blood would seem to be a logical procedure.

(*a*) *Secondary to Severe Infections.* There were three such cases. The first was a case of hemorrhagic disease of the newborn in a child whose mother had breast abscesses. The immediate result of the transfusion was brilliant. The hemorrhages stopped at once and the temperature dropped. After the transfusion, however, the temperature gradually rose again, ear suppuration set in and bleeding recurred from the mouth, skin, and intestines. The hemorrhages now were very slight and the child died of infection, not of hemorrhage.[12]

The second was a case of gonorrheal rheumatism with very severe hemorrhagic disease. The blood culture was negative, and it is not absolutely certain that the purpura was secondary to the gonorrhea. The patient's general condition which had been steadily getting worse before the transfusion, commenced to improve almost at once after it. There continued, however, to be some new hemorrhages, joint pains, etc., for about a week. The general clinical course of the disease was abruptly changed by the transfusion, and the patient ultimately recovered.

The third was a case of hemorrhagic diphtheria.[13] After the transfusion the bleeding from the nose stopped and petechiæ no longer appeared, but the toxic symptoms due to the diphtheria continued, and the patient died one week later.

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[12] This case is fully described by Schwartz and Ottenberg, AMER. JOUR. MED. SCI., 1910, cxl, 17.

[13] We are indebted to Dr. Louis Fisher for permission to refer to this case.

It is apparent, then, that in hemorrhages secondary to infections transfusion may check the hemorrhage, but that, of course, the ultimate result will depend upon whether the body overcomes the infection.

(*b*) *Secondary to Leukemia or Pernicious Anemia.* The results in leukemia in general will be discussed below, but there were 4 cases of lymphatic leukemia in which the indication for transfusion was hemorrhage from the mucous membranes. In 3 of these cases the leukemia was acute and the hemorrhages were uninfluenced by transfusion. In the fourth case the leukemia was of the chronic type, and the hemorrhages, which had not been so severe as in the other 3 cases, stopped after transfusion.

The case of pernicious anemia was one in which the hemorrhagic tendency only appeared when the leukopenia became marked (between 950 and 3000 leukocytes per cubic millimeter). Transfusion had little effect.

Aside from these cases it is possible that a peculiar form of purpura fulminans in which the polynuclear leukocytes are so greatly diminished as to almost disappear while the lymphocytes in the blood remain approximately normal or increase, is really a form of sublymphemic leukemia (perhaps better called leukopenic lymphemia). We have observed several such cases. One of them was one of the fatal cases described above under the heading of Idiopathic Purpura.

(*c*) *Secondary to Jaundice.* There were thirteen transfusions in 12 cases of prolonged obstructive jaundice. Of these cases 4 were transfused preliminary to operation to prevent hemorrhage, 7 were transfused for persistent hemorrhage after operation, and 1 was transfused simply to improve the general condition. Of the 4 cases transfused to prevent postoperative hemorrhage, such hemorrhage occurred, nevertheless, in 1. In this case a fatal intraperitoneal hemorrhage took place. Of the others, 1 died three days after laparotomy with symptoms of cholemia; the third stood the exploratory laparotomy well and died three months later. All of the 3 cases proved at the operation or autopsy to be cases of malignant disease.

The fourth case of transfusion preliminary to operation was a case of obstructive jaundice due to stone in the common duct, in which hemorrhages from the intestine leading to a marked anemia occurred before any operation was attempted. No further hemorrhages occurred after transfusion, and a successful operation was done. This was the only case in the twelve transfused for jaundice, which ultimately recovered.

Of the 7 cases of obstructive jaundice with persistent postoperative hemorrhage, 4 were due to stone or inflammation, 3 were cases of malignant disease. In all 4 of the non-malignant cases, hemorrhage from the wound continued after the transfusion as before.[14] Of the 3 malignant cases, 1 was improved by the transfusion. There were no further hemorrhages, and the patient left the hospital relieved. The second was a case in which there was an almost fatal hemorrhage from the gums and the wound two weeks after operation, with repeated small hemorrhages continuing. Transfusion, only done a month after the operation, greatly improved the patient's general condition. Repeated small hemorrhages continued, but the patient lived for three months after transfusion. In the third case gastric hemorrhage continued unchecked by the transfusion and the patient died.

Postoperative hemorrhage due to cholemia was checked then completely in only 1 case, partly in 1 other, and not at all in 5 cases. Furthermore, the precautionary transfusion before operation failed to prevent the dreaded postoperative hemorrhage in 1 of the 4 cases in which it was tried. These results are disappointing and require explanation.

The exact cause of the hemorrhagic tendency in jaundice is still a matter of dispute, but undoubtedly the changes in the viscera as well as in the blood resulting from the prolonged toxic action must be profound. One can hardly expect these changes to stop at once even after successful operation; and it would seem that the value of the transfused blood is impaired by the same toxic agencies which have already injured the patient's blood. If better results are to be obtained in these cases we shall probably have to adopt the rather bold course of a preliminary blood-letting followed by a large transfusion (two donors), so as to replace as much as possible of the patient's blood. If this is not done before operation, preparations should be made before operation so that in case of hemorrhage it can be done at the earliest moment. And finally transfusions should be repeated, if necessary.

IV. TRANSFUSIONS FOR BLOOD DISEASES. 1. *Pernicious Anemia.* There is no question connected with transfusion that has aroused more interest than that of the value of transfusion in pernicious anemia. The experiences of different observers have varied widely; while some have reported brilliant results others have condemned transfusion as useless or even harmful. With an experience of thirty-five transfusions in 25 cases of undoubted pernicious anemia we have been able to reach certain definite conclusions. (We are excluding from consideration 3 cases in which the diagnosis of pernicious anemia was not certain, 2 of which made apparent cures).

In the 25 definite cases there were no cures; 14 of them underwent more or less prolonged remissions immediately following transfusion, while 11 of them showed little or no effect.

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[14] One of these cases was transfused twice; in this case the serum of the donor was agglutinative to the patient's blood cells.

Of the 11 which showed little effect, 3 were moribund at the time of transfusion and died within a few hours or days. The other 8, in spite of marked rise of hemoglobin and temporary symptomatic improvement, showed no interruption in the course of the disease but continued to destroy their blood at about the same rate as before transfusion.

Of the 14 patients who showed progressive improvement following one or more transfusions, 1 had a remission lasting approximately three months, 3 had remissions lasting six or more months, 3 lasting a year or more, and 3 lasting over two years; 8 of the patients are alive, 3 of them less than three months, the others respectively six months, nine months, one and a half years, two and three-quarter years, and four years since the first transfusion. Of these all are in a remission stage. We believe that our results would have been still better had we been in a position to have the transfusions repeated whenever the hemoglobin began to drop.

Two patients underwent splenectomy subsequent to transfusion. In one of these the splenectomy was done after the patient had left our hands, and we only know that in general the splenectomy had little effect and the patient died a few months after it. The second was a remarkable case, already reported by Dr. Buerger.[15] In this case the first transfusion done over three years ago, at a time when the patient seemed in an almost hopeless condition (hemoglobin 18 per cent., general anasarca), was followed by a remission lasting a year, during which the patient was practically in perfect health but showed the blood picture typical of pernicious anemia remissions. Then the anemia gradually progressed again, and a year and a half after the first a second transfusion was done. The patient only held this blood for a few weeks and then again gradually became anemic, so that after three months the hemoglobin was 26 per cent. A third transfusion now raised the hemoglobin to 35 per cent., and a week later, when the hemoglobin had risen to 53 per cent., a splenectomy was done.

Since the splenectomy, the patient has been in a remission stage and she is now in excellent health. The examination of the blood on March 15, 1915, showed the following: Hemoglobin, 102 per cent.; erythrocytes, 3,660,000; leukocytes 9500; polynuclear neutrophiles, 53 per cent.; lymphocytes, 43 per cent.; mononuclears, 2 per cent.; eosinophiles, 2 per cent.; no nucleated erythrocytes or Jolly bodies;[16] undoubted tendency to macrocytosis.

Transfusion, then, so far as our experience goes, is never curative in pernicious anemia. It is a symptomatic remedy which with greater certainty than any other known remedy overcomes the chief symptom of the disease—the anemia. But it does more than this; in about half the cases it initiates a remission. It is true that remissions occur even in the most desperate-seeming cases without transfusion. But the promptness with which the remission occurred in 14 of our cases leaves no doubt that the transfusion stimulated the remission.

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[15] New York Surg. Soc., October 2, 1914.

[16] Jolly bodies had, however, been present for a long time after splenectomy.

It is well known, of course, that cases of pernicious anemia often pass early in the disease through one or two blood crises in which marked anemia is followed by a striking remission. And it might be thought that those cases in which transfusion was followed by a remission were such early cases, and that the transfusion merely coincided with the blood crisis. But an investigation of the histories of the cases shows exactly the opposite to have been the case. The cases which improved after transfusion were mostly cases which had already run a rather long course and gone through one or two crises, while the cases which failed to improve were for the most part cases of short duration. Of 12 cases whose previous histories could be fairly accurately ascertained and which showed remissions after transfusion, the average duration of the disease before transfusion was nineteen months, whereas of 8 similar cases which failed to show a remission the average previous duration was only ten months (Table I).

TABLE I.—Duration Before Transfusion of Cases in Which Transfusion was Followed by

Remission.		No remission.	
Case No. O. S. 18	3 years.	Case No. O. S. 53	6 months.
“ No. O. S. 43	3 years.	“ No. O. S. 60	6 months.
“ No. O. S. 87	3 months.	“ No. O. S. 85	6 months.
“ No. N. S. 1	1½ years.	“ No. N. S. 35	2 years.
“ No. N. S. 9	8 months.	“ No. N. S. 53	9 months.
“ No. N. S. 22	2 years.	“ No. N. S. 54	3 months.
“ No. N. S. 42	2 years.	“ No. N. S. 78	2 months.
“ No. N. S. 66	6 months.	“ No. N. S. 99	2 years.
“ No. N. S. 83	1 year.	(First transfusion.)	
“ No. N. S. 91	1 year.		
“ No. N. S. 93	3 years.		
“ No. N. S. 99	2 years.		
(Second transfusion.)			

From this we can roughly divide pernicious anemia cases into two groups: (1) chronic cases which tend to undergo remissions spontaneously and in which new remissions can be brought about by transfusion, and (2) virulent, rapidly progressive cases in which transfusion has little effect.

Aside from this we cannot say what factors determine whether a given transfusion will produce a remission or not. The size of the transfusion is not the deciding factor because remissions occurred after small as well as after large transfusions. Compatibility of the blood, in the ordinary sense, plays no role, as hemolysis and agglutination were most carefully excluded in all but 1 of our cases (this case died eight hours after transfusion). There are probably other not yet recognized differences between the bloods of donors, and we would suggest that if a remission occurs after a first transfusion an effort be made to obtain the same donor when another transfusion becomes necessary for the patient, whereas if no remission occurs a different donor ought to be tried. *In 2 of our cases in which a first transfusion failed to produce a remission a second transfusion from a different donor did so.*

It is possible that the degree of anemia which is reached before transfusion is resorted to may have something to do with determining a remission. The average hemoglobin percentage, before transfusion, of the 14 cases which showed remissions was 27 per cent., whereas the average of 9 cases which showed no remissions (excluding the 3 rapidly fatal cases) was only 20 per cent. In the former group there were 6 cases with hemoglobin of 30 per cent. or over, while in the latter there were only 2 cases in which the hemoglobin was as high as 30 per cent. This is, however, not an invariable rule, as 4 of the remission cases had low percentages (10, 13, 15, and 16 per cent. respectively) before transfusion. This observation should, nevertheless, certainly lead us to abandon our present timid habit of waiting until an extreme grade of anemia is reached before transfusing these cases.

This conclusion is further supported by another consideration. Anemia itself leads to disturbed functions or actual degenerations of viscera. Thus the persistence of a grave anemia hinders recovery from any disease, including anemia, while the mere temporary relief of anemia tends to break the vicious circle.

The effect of the transfusion on the general condition of patients with pernicious anemia is very often striking. The appetite usually improves rapidly and mental disturbances are apt to clear up. As far as our experience goes the glossitis is not directly influenced nor are, as a rule, the symptoms indicative of spinal cord involvement (except as regards the feeling of weakness which may improve with the increased feeling of strength in the entire body). In 2 cases in which we studied the gastric secretion after transfusion the achylia persisted, although the appetite and the subjective gastric symptoms improved greatly. In our last case we found that the systolic murmurs heard over the heart disappeared when the remission following transfusion was well established.

Of particular interest is the influence of transfusion on the fever, which is such a conspicuous feature of a large number of cases of pernicious anemia. It has been found in over 60 per cent. of the cases (in one report as high as 80). In 5 of the 6 febrile cases which we investigated the fever disappeared after transfusion. This phenomenon is not peculiar to this form of anemia, for among 16 other cases of anemia due to a variety of causes (excluding infections), febrile before transfusion, 8 became afebrile after it. (These included cases of gastric hemorrhage, hemophilia, splenomegaly, uterine hemorrhage, purpura, etc.). These observations lend strong support to the view that there exists a fever dependent upon anemia as such, the so-called "anemic fever."

We have in transfusion a means of determining in pernicious anemia (and probably in some other conditions) which symptoms are due to the poison of the disease and which to the anemia that is one of the results of the poison.

We may summarize our conclusions with regard to pernicious anemia as follows: *Transfusion is the best remedy for pernicious anemia; it never cures, but it leads to remissions in about half the cases;* it may repeatedly lead to remissions, but the duration of the later remissions is usually shorter than of the early ones. This is possibly due to the mere exhausting effects of protracted anemia itself. For this reason we believe that transfusion should be resorted to early instead of late, and that it should be persistently repeated as often as is necessary to keep the patient from developing a marked grade of anemia.

With regard to splenectomy, we believe from the experience up to the present time that it should be done when remissions of good duration are no longer (or not at all) obtained by means of transfusion. It may, of course, be necessary to transfuse before splenectomy if the patient is in a precarious condition. It is advisable that in patients who have been splenectomized and have had no remission, or who relapse, transfusions be tried. In this way we will learn whether the patient's life is more prolonged by initial splenectomy and later transfusions, or *vice versa*.

2. *Leukemia*. There were transfusions in 10 cases of leukemia, 9 of the lymphatic, 1 of the myeloid type; 4 of the cases were of the acute variety, with large lymphocytes predominating. In 3 of these the transfusions were without effect and the patients died in a few days. In the fourth the patient's life was probably prolonged for three months by two transfusions. In these cases there were no significant changes in the blood-picture following transfusion.

Of the 5 cases of chronic lymphatic leukemia 1 showed little change in the blood or in the clinical condition the other 4 showed along with some clinical improvement interesting changes in the blood-picture.

The first case was remarkable. It was a typical case of chronic lymphatic leukemia of a year's duration, showing, besides enlargement of the spleen and lymph nodes, peculiar skin infiltrations. The white cells numbered 120,000 and the lymphocytes 85 per cent. Simultaneous with transfusion a phlebotomy of fifty-five ounces was performed by Dr. Harold Neuhof (to whom we are indebted for the use of his notes). A month after transfusion the leukocytic blood count had become practically normal, and it remained so until the patient's death, one year later. The skin infiltrations, splenic and lymph-node enlargements, diminished for about two months, then returned, and the skin lesions developed into large tumors of the appearance of mycosis fungoides (a condition which resembles leukemic cutaneous lesions). These progressed and caused death. We are at a loss to explain the permanent change in the blood picture; it could hardly have been due to the Roentgen-ray treatment which was given from time to time.

The other 3 cases also showed marked change toward the normal, or for a time actually normal leukocytic blood pictures, but in all of them the leukemic blood picture ultimately returned. In the second case this change was least marked; the leukocytes, which had been 10,000 with 5 per cent. polynuclear cells and 95 per cent. lymphocytes before transfusion, became 4,500, with 30 per cent. polynuclears the next day, but in a week had returnəd to about the same as before transfusion.

The third patient showed a gradual change. Two days after transfusion the leukocytes had decreased from 140,000 to 66,000 and the polynuclears increased from 18 to 35 per cent. This steadily progressed until two and a half months later, when the total and differential leukocyte count was entirely normal. During this time the treatment carried on by Dr. Alfred Meyer, consisted of frequent intramuscular injections of ascitic fluid. The leukocytic blood picture remained normal (in spite of progressing anemia) for another month; then the leukemic blood type gradually returned and the patient died four and a half months after transfusion.

In the fourth case an extreme leukemic blood-picture gradually became normal a week after transfusion (concomitant with striking clinical improvement). The leukocyte picture persisted normal for a week, and then in a few days became typically leukemic again. In the one case of myeloid leukemia there was no effect on either blood picture or clinical course.

Contrary to our expectation we find, then, that transfusion does exert an influence on chronic lymphatic leukemia. The blood counts in these cases were repeatedly made, and were confirmed by several men, so that there is no possibility of error. It is true that the patients were receiving the other usual forms of treatment, but so were they before transfusion; and everyone knows how rare it is for cases of lymphatic leukemia to get a quantitatively and qualitatively normal leukocyte picture under treatment. In one of the 4 cases which showed a change it was transient and partial, and appeared immediately after transfusion. In the other 3 it appeared gradually during one or more weeks after transfusion and lasted one week in 1 case, about two months in another, and a year (until death) in a third.

It should be remembered that all these cases received only one transfusion, and that the greatest result was obtained in the case which had a rather large phlebotomy simultaneous with transfusion. We believe, therefore, that in some obscure way normal blood has an effect, and that the results of transfusion are good enough to warrant its further trial in chronic lymphatic leukemia. Such a trial should consist not of single but of systematically repeated transfusions, and we would suggest a preliminary or simultaneous phlebotomy as was done by Dr. Neuhof in his case.

V. Transfusions for Infectious Diseases. The idea of transfusion for infectious disease is almost as old as transfusion itself. Aside from the control of hemorrhage (in those cases complicated by hemorrhages), transfusion may be of use in infections, either for its general strengthening effect (particularly in protracted cases) or for some specific effect of the transfused blood. Normal blood usually has less specific bactericidal power than the blood of the infected individual, and for this reason the transfusion of normal blood probably helps only in the former way (general support). But the blood of persons who have recovered from an infectious disease or who have been artificially immunized has specific properties not only in the antibodies of the plasma but possibly also in the cells. For there is every reason to believe that in those diseases immunity to which is cellular rather than humoral the blood cells share the immune powers of the other body cells. And in this regard human blood offers the great advantage over animals' immune sera—that the blood cells transfused continue to live and functionate. Not enough attention has been paid to this possibility. We have made a small beginning in attempting to immunize a donor to the endocarditis coccus (Streptococcus viridans or mitis) before transfusion; but unfortunately most of the transfusions which we can report in infections represent haphazard trials in forlorn cases. Systematic attempts in this direction may be richly rewarded. Particularly in those diseases recovery from which confers lasting immunity, like typhoid fever, scarlet fever, and the other exanthemata, hospitals should endeavor to secure the consent of recovered patients to return and act as donors.

Aside from the typhoid fever cases (discussed above under hemorrhage in typhoid fever, and the cases of purpura complicating infectious diseases (discussed under Hemorrhagic Conditions, page 49), we can report on transfusions in 10 cases of infection with pyogenic organisms and in 4 cases of subacute streptococcus endocarditis.

1. *Infection with Pyogenic Organisms.* Of the 10 cases, 6 were due to the Staphylococcus aureus, 2 to general infection by streptococci, and in 2 the infecting organisms were not determined. All were in the most desperate possible condition at the time of transfusion, and the 4 that recovered probably owe their recovery to the transfusion.

The 2 cases in which the organisms were not ascertained were both uterine infections, the one an infected abortion, the other a case of multiple infections (so-called pyemia) following a pelvic abscess. In both transfusion had no effect.

Of the 6 cases due to the Staphylococcus aureus, 4 were cases of osteomyelitis of the femur; 2 of these recovered; 2 were cases of multiple infections (pyemia) with bone abscesses, and 1 of these recovered. All 6 cases had been ill for two months or more and were very anemic (all but 1 had a hemoglobin percentage of approximately 30 per cent.). The 3 cases that died succumbed a few days after transfusion, and indeed were moribund at the time; 1 of them died of acute hemorrhage from an eroded artery. Of the 3 cases that recovered, all had been steadily growing worse before transfusion and promptly commenced to get well after it. The effect was unmistakable, and leaves no doubt that in prolonged suppuration mere anemia and exhaustion may be all that prevent the overcoming of infection. In such cases transfusion of normal blood may offer an almost specific cure.

Of the 2 cases of general streptococcus infection, the 1 which died was practically hopeless from the start, a Ludwig's angina with multiple abscesses, complicating diabetes. The 1 which recovered was a case of (apparently) terminal streptococcus blood invasion from an unknown source, complicating a remarkably prolonged typhoid fever. (This case has already been referred to under the heading of Typhoid Fever.) In this case also it was the mere exhaustion due to prolonged fever that allowed the secondary invader to enter the blood, and the recovery after transfusion was prompt and complete.

In prolonged infection, then (due attention having been paid to surgical needs), the transfusion of normal blood may be extremely valuable and should not be too long delayed. In acute infections the value of transfusion should be determined by more extensive studies than have hitherto been made.

2. *Endocarditis.* There were transfusions in 4 cases of subacute endocarditis due to the endocarditis coccus (Streptococcus viridans, Streptococcus mitis), 1 case being in the bacteria-free stage.[17] In the 3 active cases the transfusions were done in the hope of combating the anemia and of helping the patient fight the infection. In the bacteria-free case the object was the relief of a profound anemia.

In the first case two transfusions were done. At the time the first was done the hemoglobin was 39 per cent. The hemoglobin was raised to 55 per cent. and the next day was somewhat over 60. The general condition improved remarkably, but the temperature kept up as before, and the cocci were found in the blood repeatedly. The hemoglobin did not drop to the original figure for four months, a remarkable result, because in such cases, when not transfused, once the anemia begins it becomes progressive. A second transfusion was done, using a donor who had been treated with a vaccine made from the organism present in the blood of the patient. This transfusion relieved the anemia, but the patient died a short time later from cerebral symptoms interpreted as being due to the rupture of an embolic aneurysm.

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[17] Libman, Amer. Jour. Med. Sci., 1913, cxlvi, 625.

There were two further observations made in this case that are of sufficient importance to mention here. Bactericidal studies were made of the serum of the patient and of the serum of the second donor. They were both moderately bactericidal, as was the mixture of the two. The full blood of each was also moderately bactericidal, but the combination of both full bloods was completely bactericidal. This shows that serum studies are insufficient. One should also study the plasma and the full blood if one wishes to obtain correct estimates in making bactericidal studies.

The other observation relates to a severe pain that the patient referred to the right orbit, and which disappeared promptly after the first transfusion. It did not return until the hemoglobin again was reduced to the early low figure. We were evidently dealing with an anemic neuralgia. This observation is, as far as we know, unique.

In the second case there was some improvement in the general condition, but only for a few days. The case was a very advanced one.

The third case was the only case in our entire series of a fatal accident following transfusion (aside from the two agglutinative and hemolytic transfusions discussed elsewhere[18]). A large transfusion was done and no track was kept of the hemoglobin (it was one of the early cases). At the end of the transfusion the patient suddenly showed all the signs of acute cardiac dilatation, and died a few hours later. Autopsy revealed not only extensive aortic and mitral vegetations and an unexpected tuberculosis of the lungs, but extensive miliary necroses of the heart muscle. It has never been entirely clear whether death was due to liberation of toxic substances by some lytic action of the introduced blood on the circulating bacteria or to mere mechanical dilatation of the already damaged heart muscle. The latter possibility, however, seems far more likely. Excessive transfusion is an accident which can now be easily avoided by the method of calculation which we have introduced[19] even when the transfusion is a direct one (artery to vein). Particularly in cases of cardiac disease should the amount to be transfused be carefully calculated.

The fourth case of endocarditis to be transfused was a man who had for some time been in the bacteria-free stage of the disease and who was suffering from anemia. The hemoglobin was 20 per cent., and the patient showed moderate general edema and marked edema of the feet and legs. He was put on the Karrel diet for a couple of days so that the addition of the transfused blood should not overburden his heart. The change in his condition after transfusion was very pronounced. Before the transfusion he had no appetite, suffered from insomnia, and had marked dyspnea even when walking on the level. After the transfusion his appetite returned, he slept well, felt much stronger, and was able to walk up four flights of stairs with only moderate discomfort. His dyspnea on exertion had evidently been due much more to his anemia than to his valvular disease. He eventually became anemic again and succumbed to his disease.

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[18] Ottenberg and Kaliski, loc. cit.

[19] Libman and Ottenberg, Jour. Amer. Med. Assoc., 1914, lxx, 764.

As to the advisability of performing transfusions in these endocarditis cases, we believe that they are worth trying so as to help keep the patient alive for a longer time, and so as to put the organs into better condition to respond to any methods of therapy that are tried. We believe in such cases it is advisable to test the value of repeated transfusions, especially because we now know that there is a tendency for them to become spontaneously bacteria-free.

VI. TRANSFUSIONS FOR INTOXICATIONS. 1. *Acute Poisoning.* In severe intoxications transfusion would only seem to be indicated if a considerable part of the poison is contained in or has acted on the blood. Among poisons which act in this way are carbon monoxide, hydrocyanic acid, benzol, nitrobenzol, and possibly carbolic acid. In such cases, of course, a large phlebotomy must be done before or during the transfusion.

In illuminating gas poisoning, transfusion is now accepted as the best treatment. We have seen 1 case of poisoning by illuminating gas combined with a large dose of morphin. In this case the patient recovered after the letting of a pint of blood, a large transfusion, and artificial respiration for about three hours (part of the time by Meltzer's intratracheal insufflation).

In a case of poisoning by a large dose of morphin with an unknown but probably small dose of prussic acid the same measures failed to save the patient. However, he did have a temporary return of consciousness after (although not immediately after) transfusion.

2. *Diabetic Coma.* Four cases of diabetes were transfused. The idea of trying transfusion for the relief of diabetic coma occurred to Dr. Elsberg, and the first case was transfused by him. Temporary improvement of an impending coma occurred, but three days later all the symptoms returned and the patient died. A similar result was obtained in two other cases of diabetic coma, the one complicated by a carbuncle, the other complicated by gangrene of the foot. In neither of these cases was there more than transient effect on the coma.

Transfusion was also performed in a case of diabetes complicated by pernicious anemia in a young woman.[20] Two transfusions were done in this case, each time with a marked effect on the anemia, but none on the glycosuria or the occurrence of acetone and diacetic acid in the urine. The patient subsequently died of the pernicious anemia, which was of the rapidly progressive type.

Transfusion then had no effect on diabetic coma or on the course of a severe diabetes.

VII. Transfusions for Debilitated Conditions. Now that transfusion has become a relatively easy and perfectly safe procedure, it can be applied to the relief of anemia from all sorts of causes. In cancer there is no reason to expect real benefit from it except in connection with a radical operation. A number of the cases described above under the heading Transfusions Preliminary to Operation, were such cases, and were very successful. In other wasting diseases, such as tuberculosis, transfusion may be indicated to relieve anemia and improve the general resistance of the patient.

There are many cases of simple anemia due to malnutrition or to minor causes or to no assignable cause. In some of these cases ordinary treatment is unsatisfactory or too slow, and transfusion would seem to be justified. In 2 such cases, the one anemic from no definite cause, the other as a result of repeated small losses of blood from hemorrhoids, transfusions were done with most satisfactory result.

Part III.

NOTES ON THE GENERAL MANAGEMENT OF TRANSFUSIONS.

1. *Dangers and Complications of Transfusion.* Is transfusion dangerous to the patient? The idea is still widely prevalent that it is; and yet we believe that to-day transfusion has become one of the most certain and safe of procedures. The three classes of accidents that formerly were feared—those due to incompatible blood, to dilatation of the heart, and to introduction of air—are all easily preventable by taking suitable precautions.

Accidents due to incompatibility of blood, that is to say, to hemolysis or agglutination of the red blood cells of either donor or patient by the serum of the other, have been fully discussed in a previous article by Ottenberg and Kaliski.[21] Hemolysis is by far the greater danger and was found both clinically and experimentally[22] to show accurate correspondence between the test-tube phenomenon and the occurrence in the body. *In no case in our series in which hemolysis or agglutination did not occur in the test tube were any untoward symptoms observed which could be attributed to these phenomena.*

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[20] We are indebted to Dr. Buerger for permission to use this case.

[21] Loc. cit.

[22] Ottenberg, Kaliski, and Friedman, Jour. Med. Research, 1913, xxviii, 141.

There were 3 cases in which agglutination of the donor's red blood cells by the patient's serum was observed in the test tube. Two of these patients died shortly after transfusion, and in the blood smears of both of them phagocytosis of red blood cells by leukocytes was observed. In the of these cases agglutination was the only test-tube phenomenon, in the other hemolysis as well as agglutination. In the third case the patient's serum was hemolytic to the donor's cells, and an extensive hemoglobinuria occurred after the transfusion, from which, nevertheless, the patient recovered. There was a fourth case, an emergency in which no tests whatever were made (a brother being taken as donor), and in which the patient died with convulsions during the transfusion. The patient, however, was already in bad condition (hemorrhage following nephrotomy for calculus), and it is not certain whether death was due to transfusion or not. It seems probable that it was, however, as the fatal transfusion was the second one in this case, and at the first transfusion much difficulty had occurred in finding a donor because the patient's serum was powerfully hemolytic to the blood cells of most of the donors examined.

The instances in which the donor's serum is agglutinative toward the patient's cells have been shown by one of us[23] to be theoretically far less dangerous; and, in fact, we have seen five transfusions of this kind in none of which were there any untoward symptoms or any phagocytosis in the circulating blood. We have been able to avoid transfusions in which the donor's serum was hemolytic to the patient's cells. In the great majority of cases it is possible by examining five or six different people to find one whose blood is entirely compatible with the patient's. Twice in our experience transfusion has been given up because the patient's serum was found to be powerfully hemolytic to the cells of every donor examined. In one of these instances, however, only a few donors were examined, and it is likely that if a large number could have been examined a suitable donor could have been found.

We feel absolute confidence, then, that if the tests have been carefully done nothing whatever need be feared from this source. It is needless to say that these tests require expert work and a well-equipped laboratory. They take about three hours to perform, and should never be omitted except in the most urgent cases.

The danger due to dilatation of the heart depends not only on the condition of the patient's circulation but on the amount of blood transfused and the rate at which it is delivered. When the patient's heart is known to be embarrassed, transfusion should be interrupted every few minutes. *The amount of blood to be transfused should be decided on before each transfusion* according to the principles we will discuss below. In can be controlled during a syringe transfusion by direct measurement and during a direct transfusion by the method of calculation which we have introduced.

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[23] Ottenberg, Jour. Exper. Med., 1911, xiii, 425.

We have twice seen hypertransfusions. The first case was the rapidly fatal case described above under the heading of Endocarditis. The second case was a case of pernicious anemia in which a large transfusion was performed, the hemoglobin being raised from 15 to 52 per cent. During the transfusion the patient developed all the signs of a pulmonary edema with nausea and vomiting. On the day following there was generalized edema with continued pulmonary edema and hematuria. On the third day the patient developed jaundice. She gradually recovered from these urgent symptoms, but the rapid blood destruction which had been going on continued, and she died three weeks later.

Slight jaundice occurred in 2 other cases. The one was probably an instance of Banti's disease (one of our early cases; incomplete records were kept of the case, so that it was not included in the tabulation of the present series). We believe that the jaundice was probably due to the same cause (excessive transfusion) possibly accentuated by the special hemolytic tendency of the disease itself. In the other case in which a slight jaundice followed transfusion the patient was suffering with a carcinoma of the stomach with numerous metastases.

Hematuria also occurred in 1 other case. It was a case of nephritis with uremia and anasarca. This case was not discussed above under the subject Indications for Transfusions. A phlebotomy of 400 cubic centimeters was followed by a very large vein-to-vein transfusion. It was impossible to follow the amount of blood being transfused by the calculation method because the patient's and donor's hemoglobin were practically the same at the start. Transient hematuria occurred which may have been due to excessive transfusion, but more likely to a special permeability of the kidneys from nephritis, since red cells were found in the urine also at other times independent of the transfusion.

Aside from these unfavorable reactions due to incompatible blood or to hypertransfusion, a more or less marked febrile reaction occurred in about 10 per cent. of all our cases, and skin eruptions, usually urticarial in character, occasionally a few petechiæ, appeared in another 10 per cent. In no instance were these symptoms serious, and in every case they cleared up within three days.

2. *The Donor.* The securing of donors always offers a certain amount of difficulty on account of the necessity of examining a number of men in order to be certain to find someone whose blood is compatible with that of the patient. We have generally inserted an advertisement in the newspapers. Occasionally relatives of the patient have been used, but, as has been shown elsewhere,[24] it is

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[24] Ottenberg and Kaliski, loc. cit.

quite as necessary to make the blood tests of relatives as of strangers. In New York there is never any lack of response to advertisements, and we make a practice of keeping a reserve list of men who have answered such advertisements and who can be reached by telephone or otherwise, for use in emergency transfusions. The applicants never object to the taking of about 5 c.c. of blood for hemolysis tests and Wassermann reaction. Sometimes a small stipend is given to them for allowing this to be done.

It is important to know what to tell donors and what can be promised them. They can freely be promised absolute safety and a minimum of pain. When a syringe transfusion is to be done they are able to go to work again the next day. When a direct transfusion is done the wound hampers work for a week or two and in these cases the amount of money paid the donors is usually larger. We have only once known the donor to have any subsequent trouble from transfusion. This was due to an infection of the wound, caused by his own carelessness. In the great majority of instances the recovery of the lost blood by the donor after transfusion is surprisingly rapid, and several donors have been in perfect health and have been used again for transfusion a month or six weeks after the first transfusion. *It is wise in every instance to have the donor before the transfusion sign a legal form, relieving the patient and the surgeon from further liability, and stating the amount of money that he is to receive.*

Aside from the blood test a physical examination should be made to rule out infectious disease (especially tuberculosis and syphilis) or any cardiac condition which would contra-indicate the use of a particular donor. The physical build and temperament of donors are to be taken into consideration. Large men (weighing one hundred and sixty-five pounds or over) are to be preferred, as more blood can be taken from them with safety. Very fat men are not desirable, because in proportion to their weight their blood volume is less. Men of nervous or timid temperament should not be taken, as their actions are likely to interfere with the success of the transfusion. For syringe transfusions the character of the superficial veins is important.

The watching of the donor during transfusion is more important in direct than in syringe transfusions. The donor should be given fluids, such as soup and hot coffee, but whisky should be avoided, as it frequently causes vomiting and does not seem to do any good. The actions of different men during the loss of blood is exceedingly variable, and for this reason the observation of the donor is not a very reliable guide in transfusion. The pulse more frequently becomes slow than rapid. Toward the end of the transfusion it usually becomes soft, sometimes dicrotic. If the pulse rate becomes less than sixty it is best to stop the transfusion. Often the appearance of the patient is unchanged until a sudden collapse occurs.

Sometimes repeated yawning occurs toward the end of the transfusion, as an indication that enough blood has been taken. The first signs of collapse are sweating and pallor, and when these occur a real collapse almost invariably follows, with thready or imperceptible pulse, semiconsciousness, and vomiting. Recovery usually takes place without any special stimulation. We have only once seen a severe collapse that required active steps to be taken. This was a transfusion in a case of shock due to typhoid perforation in which an unusually large transfusion was done, and on account of the patient's desperate condition little attention could be paid to the donor. However, with stimulation the donor recovered in about a half-hour and had no further trouble. In a number of instances large amounts of blood (three pounds or more) are known by actual weighings to have been transfused without causing serious trouble.[25]

If sufficiently long periods are allowed for the hemoglobin percentage to reach the normal again the same donor can be used for repeated transfusions, and there are certain advantages in doing this.

3. *The Technic of Transfusion.* What is the best method of performing transfusion? This is not the proper place to enter into an extended discussion of questions of technic, but since the technic often plays a very important part in determining whether a transfusion should be done or not we will briefly consider the advantages of the several methods. The syringe method, as practised by Lindeman, possesses great advantages over other methods. It involves no trauma and very little pain, and thus does not add the shock of a surgical procedure to the burden of an already sick patient. The exact amount transfused is always known. Not the least advantage is that syringe transfusions can be done repeatedly on the same patient as often as desired. This opens all sorts of new possibilities in transfusion therapy. To some it will appear to be a disadvantage that the syringe method requires a more expensive apparatus. This, however, is no real obstacle. The aspiration of blood from the donor should not be left to an untrained assistant, as this part of the procedure is quite as difficult as the injection into the patient.

The disadvantage of the direct transfusion is that it is a cutting operation and destroys a vein of the patient, so that only a limited number of repeated transfusions can be done. When the patient does not have a low percentage of hemoglobin at the start of the transfusion it also has the disadvantage that one cannot estimate how much blood is being transfused. We believe that those undertaking to do transfusions should be skilled not only in the use of the syringe method, but also in the direct method conducted by means of the Elsberg cannula or Carrel suture. It may be necessary at times to use one of the latter methods.

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[25] Libman and Ottenberg, loc. cit.

We have had no experience in the use of anticoagulants, such as hirudin and sodium citrate. In hemorrhagic diseases, which constitute so important a part of the indications for transfusion, such anticoagulants would seem to be contra-indicated. Dr. Richard Lewisohn (personal communication) has made studies of the value of hirudin added to the blood to be transfused and finds it to be not harmless.[26] There are reports that sodium citrate can be used without danger. The method of defibrination is open to the same objection in hemorrhagic conditions as the use of anticoagulants—namely, that it removes fibrinogen and blood platelets. Moreover, it is impossible to defibrinate blood without mechanically injuring the red blood cells to a certain degree, and there is a possibility that if a large amount of defibrinated blood is transfused the antithrombin of the patient's blood will not be sufficient to neutralize the action of the thrombin in the defibrinated blood and that intravascular clotting will occur.

In the great majority of the transfusions reported in the present paper the direct method—artery-to-vein or vein-to-vein—was used. In about twenty of the later transfusions the syringe method was used.

4. *Amount of Blood to be Transfused.* The quantity of blood to be transferred should always be determined beforehand by consideration of the following data:

(*a*) The weight of the donor.
(*b*) The weight of the patient.
(*c*) The condition of the patient.
(*d*) The nature of the disease.

The first two factors have been discussed by us in a previous paper.[27] The third has been considered above under Dangers in Transfusion. As far as the nature of the disease influences transfusion the following conditions may be considered:

1. *Hemorrhage.* In hemorrhage an effort should be made so far as possible to replace the lost blood. Experience, however, shows that collapse can be overcome and the patient brought into a condition of safety by a smaller amount than has been lost.

2. *Hemorrhagic Diseases.* In hemorrhagic disease a relatively small transfusion (500 c.c. for an adult) is usually enough unless the amount of blood already lost has been very large. In hemorrhages due to cholemia we believe that a large transfusion with perhaps a preliminary phlebotomy is indicated (see Cholemia).

3. *Anemias.* When it seems desirable to raise the hemoglobin to a given point it is important to remember that there is generally a rise of the hemoglobin within twenty-four hours to a percentage somewhat higher than that at the end of the transfusion. We have observed this in the majority of our cases in which there was

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[26] Dr. Lewisohn believes that various preparations of hirudin vary in toxicity.

[27] Libman and Ottenberg, loc. cit.

no hemorrhage after the transfusion. Generally the rise is about 5 per cent., but sometimes it is as high as 10 per cent. It is presumably due to a concentration of the blood. In pernicious anemia a moderate-sized transfusion (500 c.c. to 1000 c.c.) is probably sufficient.

4. *Poisoning.* In the various forms of poisoning, especially in gas poisoning, a large phlebotomy followed by a very large transfusion would seem to be indicated.

5. *Repetition of Transfusion.* As suggested above, there are probably many conditions in which repeated transfusions will accomplish a great deal more than a single large transfusion, or in which the repetition of transfusions may become necessary at later stages of the disease. Some such conditions are pernicious anemia, hemophilia, and infections, whether local or general. There is no danger in repeated transfusions provided the tests for hemolysis and agglutination are carefully done. The likelihood of hemolysis occurring is distinctly greater in the second and third than in the first transfusions, due to the development of immune hemolysins. We have found this experimentally,[28] and several of the cases of fatal hemolysis after transfusion reported in the literature are instances of second transfusions. In 21 of our cases there were two transfusions, and in 3 of them three transfusions, without any special ill effects.

ADDENDUM. Unger[29] has eliminated the difficulties experienced in the Lindeman method by the use of a simple apparatus. Up to the present time his apparatus has been used in twenty cases. Transfusions can be performed very rapidly, 60 c.c. on an average being transferred per minute. Chills, rises of temperature, vomiting and other symptoms that are occasionally seen after transfusions, seem to be less frequent when this method is used than when either the Lindeman or citrate methods are used. We can regard Unger's method as at present the best for direct transfusion.

Hustin,[30] of Brussels, in May, 1914, published animal experiments in which citrate of soda was used and citrate of soda mixed with glucose. He stated that he had successfully used in one human case a mixture of blood and saline solution containing citrate of soda and glucose. He diluted the blood with an equal amount of saline solution because he feared that the 0.2 per cent. strength citrate which he was using in the blood might be dangerous if the blood was not diluted. This method would limit the size of transfusions and apart from that more recent studies have shown that such dilutions and the use of glucose are not necessary. At a meeting at the New York Academy of Medicine at which the present writers communicated some of their studies, Weil stated that he had successfully done transfusions in human beings using a 1 per cent. strength of citrate of soda and transferring amounts of blood up to 250 c.c. The coagulation time of the blood of the patients was not prolonged, in fact shortened.[31] Lewisohn[32] has reported the successful use of citrated blood in large amounts using only 0.2 per cent. of the salt. He feared that the percentage of citrate used by Weil would be toxic when large amounts of blood were transfused.

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[28] Ottenberg, Kaliski, and Friedman, loc. cit.

[29] Jour. Am. Med. Assn., 1915, lxiv, 582.

[30] Ann. et Bull. de la Soc. Royale de Sci. Méd. et Nat. de Bruxelles, 1914, No. 4, p. 104.

Weil believes that the great value of the citrate method lies in the fact that the blood may be kept on ice for a number of days and repeated injections of small amounts used. He has done 200 transfusions in 46 cases.[33] He usually injected 300 to 350 c.c. of blood, but in one case he used 1400 c.c. The strength of sodium citrate was 1 per cent., occasionally 0.3 per cent. The blood was used as late as six days after it was obtained, but usually within three days. The reactions after transfusion were unimportant. There was occasionally chilliness and headache. In six cases the temperature rose to 102° F. and in four cases, above 102° F. Polyuria occurred frequently. The patients seemed to hold the blood well. The coagulation time was frequently cut in half very shortly after the transfusion, but returned to the original time within twenty-four hours.[34]

Lewisohn has transferred 25 cases; the highest amount given at one time was 900 c.c., but in one case 1600 c.c. were transfused within twenty-four hours. There was a diuresis in most cases which stopped within twenty-four hours. Some patients suffered from headache, and some perspired profusely. He has confirmed all of Weil's observations concerning coagulation time. It is important that he has found that the solution can be sterilized without losing any of its value. In three of his cases a chill resulted and in five there was marked temperature reaction. The chills occurred less frequently, however, than they occurred in Lindeman's series.

We have seen all these newer procedures used and believe that the method of Unger and the citrate method are at present the methods of choice. For large transfusions many will prefer the Unger method. The citrate method has distinct advantages when one wishes to make repeated injections of blood. Apart from its great simplicity it will be of particular value when patients live at a distance or when it is desirable that the patient does not realize that an important procedure has become necessary. If future studies demonstrate that citrated blood acts as well in pernicious anemia as uncitrated blood and if no disadvantages are found from its repeated use in cases of hemorrhagic disease, this method will prove the most widely applicable.

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[31] Weil, Med. Rec., New York, January 23, 1915, lxxxvii, 164; see also Jour. Amer. Med. Assn., January 30, 1915, lxiv, 425.

[32] Med. Rec., New York, January 23, 1915, lxxxvii, 141.

[33] These facts were presented by Dr. Weil in a communication made to the American Society for the Advancement of Clinical Investigation, May 10, 1915.

[34] Dr. Lewisohn's publication will appear shortly in the Journal of Surgery, Gynecology and Obstetrics. We are indebted to both Dr. Weil and Dr. Lewisohn for giving us these facts in advance of their publications.

GASTRIC GLANDS IN MECKEL'S DIVERTICULUM.[1]

By G. R. Callender, M.D.
FIRST LIEUTENANT, MEDICAL CORPS, UNITED STATES ARMY.

Some time ago the writer performed an autopsy on a child aged nineteen months, who had died as a result of intestinal hemorrhage. There was a history of one previous attack from which it recovered, but had always been rather weak and ill nourished.

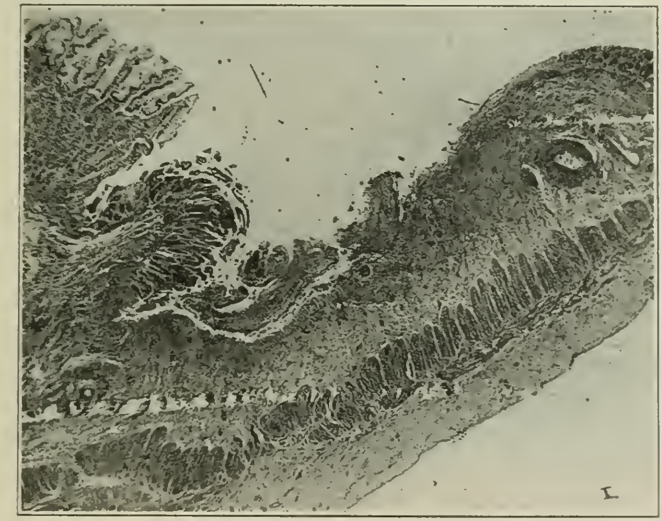

Fig. 1.—Low-power picture showing, from left to right, gastric type glands, villus of ileum, ulcer, and ileal mucosa. The artery at the right is a section of the vessel that ruptured.

At autopsy the skin and mucous membranes were pale, as were all the internal viscera. With the exception of the intestine the latter showed nothing remarkable.

Intestine. About 75 cm. from the cecum on the border of the ileum opposite its mesenteric attachment was a diverticulum, 2 cm. in length and 2.5 cm. in diameter, attached to the posterior wall of the cecum at its apex by a fibrous band 0.4 cm. in width. On section there appears a punched-out, regular ulcer, 0.5 cm. in diameter, in the ileum at the border of the diverticulum. In the margin of this ulcer is a small vessel, the lumen of which is plugged with pinkish clot.

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[1] Published with the permission of the Surgeon-General, United States Army.

The walls of the diverticulum are from 0.4 to 0.6 cm. in thickness, and the mucosa resembles that of the fundus of the stomach. There was no macroscopic blood in the intestine. Death did not occur until thirty-six hours after the hemorrhage, and the movements had ceased to contain blood for twelve hours.

Microscopic examination shows an ulcer extending through the mucosa. The base of the ulcer is made up of a dense layer of fibrous connective tissue infiltrated with polymorphonuclear leukocytes and lymphoid cells. Section taken through the blood-vessel shows it to be a small artery filled with a relatively acellular, fibrinous thrombus. A section through the ulcer, and extending into the diverticulum, shows from the border of the ulcer, first a layer of ileal glands, then with a rather sharp demarcation, superficial glands having no goblet cells but epithelium of high columnar type with clear peripheral cytoplasm. This epithelium extends to the bases of crypts into which simple tubular glands empty by narrow mouths. These latter glands form a thick layer extending to the musculosa, and are lined by two types of cells, as in the fundal glands of the stomach. The chief, central, or adelomorphous cells are of low columnar or pyramidal shape, stain rather faintly with eosin, and contain relatively few granules. The parietal, acid,

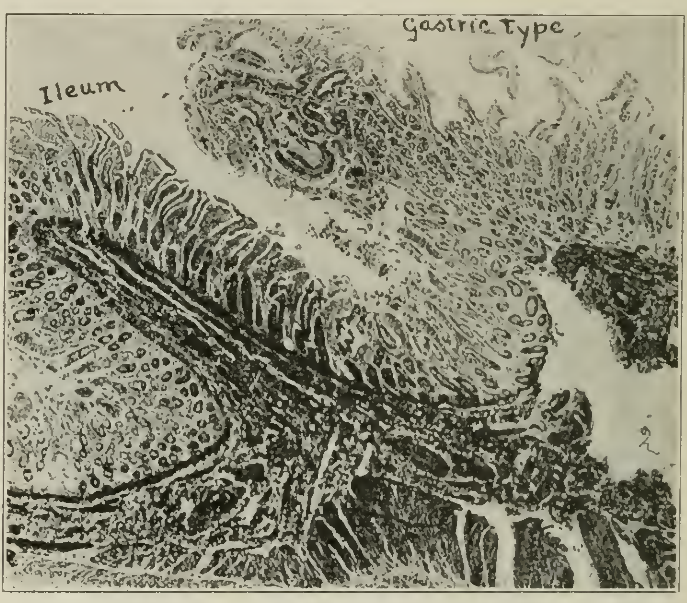

Fig. 2.—Intermediate power, showing junction of mucosa of gastric type with that of the ileum.

oxyntic, or delomorphous cells, largely at the peripheries of the glands on the basement membrane, take the eosin stain deeply and are filled with fine granules. The musculosa consists of two layers, an inner circular and an outer longitudinal.

Diagnosis. Peptic ulcer of the ileum; Meckel's diverticulum, lined with mucosa of the type of the gastric fundus glands.

Remarks. The usual structure of Meckel's diverticulum is that of the ileum: two thin layers of muscle and a mucosa made up of few villi and crypts of Lieberkühn, with occasional areas of lymphoid tissue. They are found about 80 cm. from the ileocecal valve, and are formed by the incomplete closure of the vitelline duct.

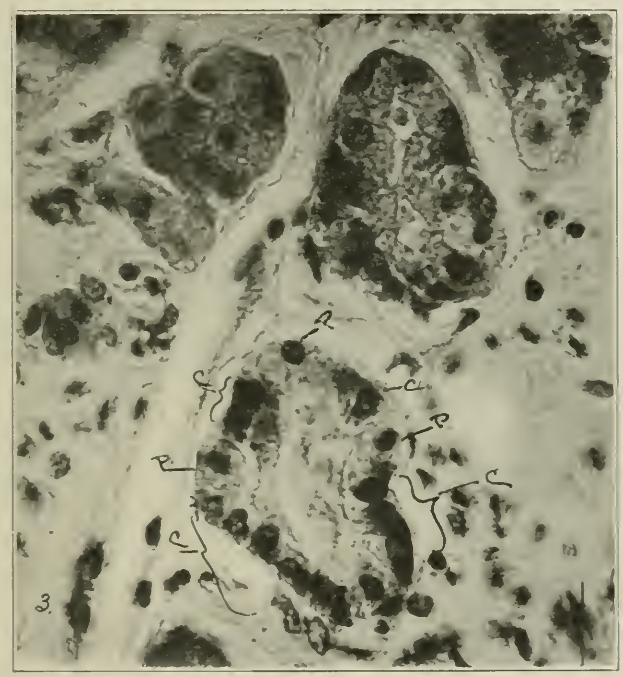

Fig. 3.—High power, showing (*C*) chief and (*P*) parietal cells of the tubular glands. (Stain, eosin-methylene blue.)

A search of the literature revealed no similar case. Hedinger,[2] in 1906, reported a case in which there was an island of pancreatic tissue intermingled with Brunner's glands at the apex of a Meckel's diverticulum.

Acknowledgement is due Doctor C. A. Riley, of Allston, Massachusetts, through whose courtesy the writer was enabled to perform the autopsy.

[2] Corr.-blatt. f. Schwiez. Aerzte, Basel, 1906, xxxvi, 395.

GASTRO-INTESTINAL STUDIES, NO. X: AN ANALYSIS OF ACHYLIA GASTRICA.

By Martin E. Rehfuss, M.D.,
PHILADELPHIA.

(From the Departments of Physiological Chemistry and the Practice of Medicine of the Jefferson Medical College, Philadelphia.)

Achylia gastrica stands at the bottom of the long list of secretory disturbances as the expression of the total lack of both enzymes and secretion. Various authors have tried to picture a characteristic clinical syndrome, but the fact remains that the recognition of achylia gastrica can only be made through a direct examination of the intragastric mechanism. This means that an examination of the gastric contents is absolutely essential, although some observers claim that its presence can be recognized by fecal examination. In a summary of the many contributions to this subject, it is evident that the time-worn method of the administration of the test meal and its removal in one hour have been employed. This means that the commonest of all misdiagnosed conditions in this field can scarcely be separated. I refer to the spurious achylias which I shall discuss in the latter part of this article. The introduction of the functional method opens up a new line of study in this field. It enables us to follow the transit of food through the entire cycle of gastric digestion into the duodenum, and there we find a more or less characteristic observation in true achylia, namely, the passage of food into the intestine which is similar in every way to that merely macerated by saliva, for instance, and not chymified. In a true achylia, and speaking broadly I mean a complete achylia, there is no evidence of gastric secretion in any phase of gastric digestion. Not only is there no free hydrochloric acid and practically no total acidity, but pepsin and rennin are lacking. This is rarely the case in gastric neoplasm. Today from the classical studies of Pawlow as well as many other observers we divide the gastric secretion into psychical and chemical phases. The psychical secretion we have been able to demonstrate with normal individuals. If this be true, therefore, that there is a definite psychical secretion initiated through the pathway of the vagus, whose tonus is probably maintained by certain internal secretions (probably parathyroids (?) and possibly thyroids (?)), and a definite chemical secretion incident to the formation and absorption of substances elaborated in the course of digestion, so-called secretagogues and hormones, it should follow that suppression of either of these phases should lead to a psychical or chemical achylia. The investigation of the entire gastric phase would then give us information as to the possible failure of one or the other of these secretions. A total absence of secretion during the first hour of digestion followed by a perceptible secretion in the second would favor this view-point, namely, that a psychical achylia (nervous) exists, the reverse a pronounced secretion during the psychical phase would favor the interpretation of a chemical achylia. A total lack of secretion through both phases might indicate a deficiency of both functions, or an inactive mucosa, or possibly the failure of material in the blood from which the gastric secretion is derived.

Our studies have indicated that in the majority of cases a complete achylia occupying both phases occurred. We have, however, found several cases in which there was a manifest achylia for one hour or more followed by a perceptible secretion in the second phase, namely, a true nervous or psychical achylia. The reverse, a chemical achylia we have never encountered.

Until we know fully the mechanism and actual formation of the gastric juice, the definite causes producing these secretory phenomena must escape us. It is of interest to note, for instance, that after parathyroidectomy, Carlson and Keating[1] were able to demonstrate a marked deficiency in gastric secretion which was aided and improved by calcium salt administration. On the basis of this observation, in two cases of pronounced persistent achylia of long duration, one of them over ten years, we were able to demonstrate a perceptible and distinct return of secretion during the first hour of digestion. Dr. Bergeim, in our laboratories, elaborated an interesting hypothesis on the origin of gastric hydrochloric acid.[2]

According to this hypothesis the hydrochloric acid is formed from the NaCl of the blood through the interaction of this substance with an acid phosphate in the gastric cells. It was suggested that the acid phosphate was more probably the Ca acid phosphate than acid Na phosphate, because *in vitro* it is much easier to decompose NaCl by the action of the Ca salts. This is due to the fact that the acid Ca phosphate readily hydrolyzes with the formation of a basic Ca phosphate and free phosphoric acid, while the Na salt does not do this. According to him the formation of such an acid salt in the gastric cells presents no great theoretical difficulty, as organic P compounds, particularly nucleic acids, are found in all tissues, and are associated with enzymes capable of splitting off the phosphoric acid. Further, the nucleic acids appear often to exist in combination with Ca. According to this view, the organic P compound may be furnished by the blood. The findings of high acidity and efficient digestion associated with hyperfunction of pituitary and thyroid and the opposite in hypofunction, as well as decrease in secretion after parathyroidectomy, are interpreted to indicate an influence of these glands over the mobilization and decomposition of the organic P compound.

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[1] Keeton, Amer. Jour. Physiol., 1914, xxxiii, 25.

[2] Proc. Soc. Exp. Biol. and Med., 1914, xii, pp. 21–22.

This question is worthy of extended study and investigation, and is mentioned owing to its interest and importance in connection with the cases which we report here.

Discussion of Cases.—The results in these cases are recorded in terms of $\frac{N}{10}$ NaOH, the pepsin was tested by the mett method, and in cases where rennin is marked absent, undiluted content failed to act on milk.

Case I.—Mr. E., patient, was a perfectly healthy young farmer up until a short time before admission into the hospital, when he developed trouble with the ankle-joint and knee-joint on the left side; the patient otherwise was in perfect health, and said that his stomach in no way bothered him. The tube was passed and retained, and specimens removed at fifteen-minute intervals. In one and a half hours after the administration of an Ewald meal the stomach was found to be empty and the rapid motility characteristic of that condition was found to be present. Patient's nutrition was satisfactory and the intestines were able to maintain, to a remarkable degree, their vicarious function.

Time.	Total acidity.	Free acidity.	
15 minutes	1.0	0	
30 "	1.5	0	
45 "	2.5	0	no enzymes
60 "	2.5	0	
90 "	3.0	0	

These figures are practically equivalent to a total absence of all secretion, and the enzymes were lacking. A study of the specimens collectively and separately showed no mucus, no blood, no evidence of any pathological cytology, in fact, nothing but a wet achylia with absolutely no evidence of inflammation. In this case the whole phase shows achylia, and in the absence of any evidence of inflammation, fermentation, bacterial action, and any local or constitutional disturbance incident to the gastric condition, I can only consider the condition a glandular one. Unfortunately, further studies were impossible. Vicarious intestinal function was almost complete.

Case II.—Mrs. B., aged fifty years, four months loss of appetite; loss of weight; pain in the epigastrium, and in fact everything which suggested gastric carcinoma; no palpable mass; no vomiting. This case, which is of great interest, was in the service of Dr. Solis Cohen, in the Jefferson Hospital, and it was with his kind permission and coöperation that I was enabled to study the case. Owing to the lack of appetite and the epigastric pain, the patient had refrained from eating and lost considerable weight.

Examination revealed a soft, rather relaxed abdomen, in which the stomach could be distinctly outlined by inflation extending to the level of the umbilicus, absolutely free from any palpable masses, and in which no tender points could be palpated; nor was there any splash or clapottage. The passage of the fractional tube on the empty stomach failed to reveal any appreciable residuum, and there was no retention or food rests, and no hypersecretion. An Ewald meal was then given, and after the first few samples, which were rather liquid, material having all the characteristics of a dry achylia was removed. The material was removed at intervals until the one and three quarter-hour interval, when the stomach was found to be empty—a lavage confirmed this finding. The results of this first examination are as follows:

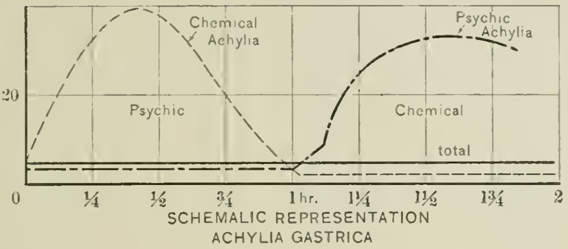

FIG. 1

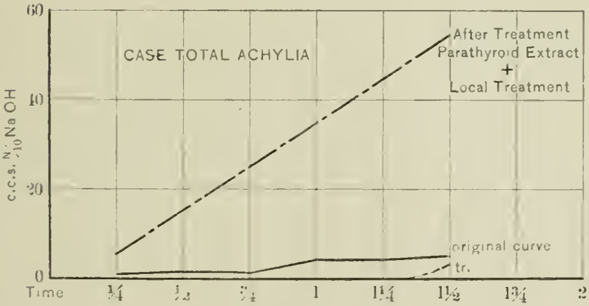

FIG. 2

Time.	Total acidity.	Free acid.
20 mins.	1.0	0
30 "	3.0	0
40 "	2.5	0
1 hour	1.0	0
1¼ hours	4.0	0
1½ "	4.0	0
1¾ "	low	0

This was repeated three days later with the same findings. An examination of different portions revealed neither pepsin nor rennin, nor was there mucus, occult blood, or bacteria in any of the specimens. The albumin reaction did not exceed $\frac{1}{80}$ in any phase, and there were no cytological findings, no lactic acid was found, and absolutely no signs of putrefaction. I was compelled, on the strength of this examination, to make a diagnosis of benign achylia, and shortly after Roentgen-ray examination revealed absolutely nothing in the stomach. Examination at that time revealed a small palpable mass in the inner aspect of the cecum corresponding to the appendix, and toward this were peristaltic waves, small intestinal, indicating a probable obstruction in this region. An achylia diet was instituted; the patient was given parathyroid extract, and shortly afterward commenced to gain weight. In a comparatively short times her appetite had returned.

A second test several weeks after the first observation revealed the following curve:

Time.	Total acidity.	Free acid.
5 mins.	7.0	0
15 "	15.5	Trace
30 "	11.0	Trace
45 "	3.0	0
1 hour	8.0	0
1¼ hours	....	0

Shortly afterward she continued to improve, and in the interval gained seven pounds, was free from pain, and eating liberally. Her subsequent history was not so satisfactory; shortly afterward she suffered from grippe and was readmitted into the hospital in very bad shape; marked headache; severe pain in the back; lassitude; and a mass in the right side; 23,000 leukocytes; probable carcinoma of cecum, with infection and abscess formation. Her condition was so poor as to prohibit intervention, and she died, without permission from the family for an autopsy. Of one thing I am certain, that in this case the gastric sumptoms were not due to carcinoma ventriculi. The mass in the right side was small and insignificant, and was probably an early carcinoma of the cecum. In this case all the improvement, as shown in two examinations, was on the psychical side of the curve—no improvement was noticeable later in the curve—and the case is of interest as registering a distinct improvement under parathyroid.

Case III.—The following case was a very intelligent gentleman, M. P., referred to me by Dr. Nylin. To all intents and purposes he was perfectly healthy, and there were no gastric symptoms whatsoever. He complained only of looseness of the bowels, from which he had suffered for many years; it was scarcely looseness, rather than an undue frequency of the bowels. Careful examination showed high blood-pressure 160, accentuated aortic, very early signs of interstitial changes in the kidneys, some gouty tendency. Examination of the movement showed a malassimilation of carbohydrates and connective tissue in small amounts. His curve was as follows:

Time.	Total acidity.	Free acid.	Pepsin.	Rennin.
15 mins.	3.1	0	0	0
30 "	3.1	0	0	0
45 "	3.0	0	0	0
1 hour	6.0	0	0	+
1¼ hours	4.0	0	+ trace	++
1½ "	23.0	Trace	0.5^2	++
1¾ "	31.0	Trace		

This case is extremely instructive. It shows according to the ordinary technique, an achylia, but by the fractional method it shows a total psychic achylia, distinct evidence of a chemical secretion during the second phase. This has been endured for years, and yet there was absolutely no evidence of any irritation on the part of the stomach, no bacteria, mucus, or blood—simply a dry achylia, from which juice was filtered, with difficulty in the first phase and distinctly more abundant in the second phase. Furthermore, evidence of both pepsin and rennin were found throughout later phases.

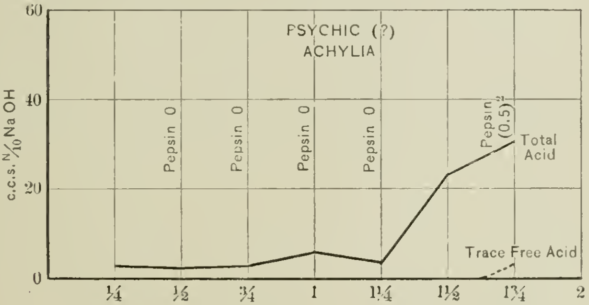

FIG. 3

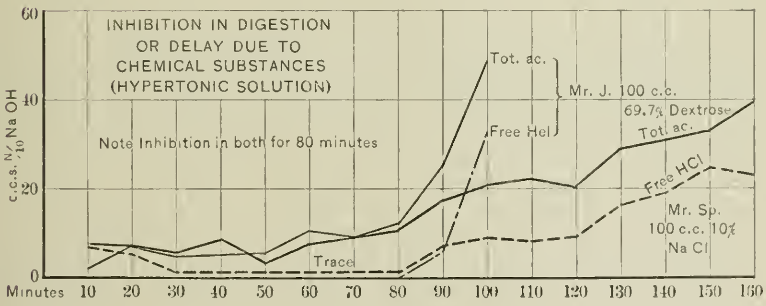

FIG. 4

CASE IV.—Mr. K. was referred by Dr. Beardsley and Dr. Tracey, Beverly, New Jersey. This case was one of unusual interest, inasmuch as it presents the many phases and causes which might be operative in causing an organic achylia and in which a bad prognosis was fortunately incorrect. Mr. K., aged forty-seven years, hard worker, and exposed to considerable nervous tension, has been suffering for many years from an obscure gastric condition. Ten years ago, when seen by Dr. Musser, he was found to have an achylia with gastric catarrh and dilatation. At the time when I first saw him his condition was deplorable, his appearance a grayish green, and markedly anemic. He complained of bringing up a small amount of yellowish mucus every morning. His condition to the attending physicians suggested a pernicious anemia, and I must confess that it seemed that such a course was likely, although a complete blood picture and certain signs were atypical. Wassermann was negative, and before I made a gastric study, another physician had made an examination, found a great deal of pus and mucus in the stomach, and a complete achylia according to the ordinary methods. The empty stomach revealed little retention, but a great deal of mucus, and the fractional examination after the administration of the Ewald meal showed the following:

Time.	Total acidity.	Free acid.	Mett pepsin.	Rennin.
5 mins.	1.0	0	0	0
15 "	1.0	0	0	
30 "	1.5	0	0	
45 "	1.5	0	0	0
1 hour	4.0	0	0	
1¼ hours	4.0	0	0	
1½ "	5.0	0	0	0

Total achylia in every phase, an enormous amount of mucus, pus which had been clearly swallowed, many bacteria, some swallowed and others intimately mixed with the contents; *no enzymes;* absolutely no response, and tinged throughout in each case with blood. Neoplasm ruled out, owing to the duration, the relatively low loss in weight, absence of mass, and of any Roentgen-ray findings and the diagnosis of achlorhydria hemorrhagica gastrica secondary to ingestion of infected mucus from probable bronchiectosis in lung. To make a long story short, diet was immediately regulated, lavage and the direct local application of silver was carried out, iron and arsenic given hypodermically, and parathyroid given, gr. $\frac{1}{10}$, t.i.d., for three days at intervals. After three months he had gained twelve pounds in weight, his blood had gone up to 4,200,000, his hemoglobin over 80 per cent., his appetite had completely returned, but the important thing was the gastric analysis, after an achylia of ten years' duration, in which we all felt justified in believing there was an atrophic gastritis:

Time.	Total acidity.	Free acid.	
15 mins.	6.0	0	
30 "	....	0	
45 "	15.0	0	
1 hour	35.5	Trace	Pepsin present.
1½ hours	55.0	Strong trace	Free acidity.

Rennin—not tested.

Still some mucus, but infinitely less than on former occasions, and a few bacteria which have been gradually stamped out. I am not prepared to believe that the parathyroid is entirely responsible for this change. In fact, the hypodermic administration of hematinics may have wrought a change; furthermore, I acted on the principle that nutrition was the important thing in his case, increased assimilation being followed by marked improvement. Among the interesting points in this case was the return in the salivary secretion to which the patient himself called attention; furthermore, the tongue, which was glossy and rather pale at first, became bright red, with papilla distinct. The bowels, which were markedly constipated, phenomena of mucus colitis being frequent, were once more regulated, although it must be confessed a small amount of magnesia was and is being used. It is my belief that parathyroid is in part responsible for the return of the secretion, inasmuch as qualitative tests on other occasions did not reveal such a pronounced effect. The gain in weight was from 131 to 158 pounds, and at this writing, nine months later, the cure is complete.

Case V.—Represents Mrs. Si., aged thirty-eight years, who has been suffering for three years with nausea and vomiting and an obscure gastric affection which suggested neoplasm. Her curve shows an absolute achylia in every phase and no enzymes. Abderhalden reaction was negative, and Roentgen-ray studies show, outside of marked ptosis of both stomach and large bowel, no evidence of any neoplastic condition. Stool examinations show connective tissue which has come through, but otherwise poor utilization of fats. The case exhibits also hyperthyroidism, and is at present under observation. There is undoubtedly a marked catarrhal process present, and two examinations at an interval of two weeks reveal complete achylia:

Time.	Total acidity.	Free acid.	Pepsin.	Albumen.	Rennin.
5 mins.	2.0	0.0	0	..	0
10 "	2.5	0.0	0	80	0
15 "	3.0	0.0	0	..	—
30 "	4.0	0.0	0	..	—
45 "	4.45	0.0	0	..	—
1 hour	6.0	0.0	0	80	0
1¼ hours	5.0	0.0	0	..	—
1½ "	10.0	Trace	0	80	? 30 min.
1¾ "	9.0	?	0		

Gastric mucus in every specimen.

Digestion of an Ewald meal is over in one and three quarter hours. It will be seen that there is practically no elaboration of acid; there is, however, a trace to be found in the more advanced stage of digestion. There is a large amount of mucus, illustrative of a pronounced catarrh. The question which arises is naturally that between a neoplasm, a benign achylia, and a pronounced infected gastritis (achlorhydria hemorrhagica gastrica). Against the former is the blood count, the condition of the patient, the peculiar type of the albumin curve, which in that condition steadily increases. Furthermore, there is to be found no lactic acid, no Oppler-Boas bacilli, but some small diplobacilli and bacteria.

Case VI.—Contrast the preceding with the following case of spurious or false achylia in a case of marked gastric catarrh.

Mrs. H., suffered from typical loose bowels—with apparently no definite cause, indigestion, discomfort, eructations after eating. Occasionally cramp-like pain in the upper abdomen. Empty stomach negative, except for small residuum almost entirely composed of gastric mucus.

An Ewald meal gave on fractional examination the following results:

Time.	Total acidity.	Free acid.		
5 mins.	2.0	0	Mucous	
10 “	2.0	0	Mucous	
15 “	3.5	0	–	
30 “	4.0	0	–	
45 “	4.0	0	–	—pepsin +
1 hour	5.0	0	–	—pepsin +
1¼ hours	3.5	0		
1½ “	15.5	0	–	—pepsin +
1¾ “	23.6	0		Rennin—not tested.

Here was a case of chronic gastritis with hypermotility and the typical gastrogenous diarrhea incident to a lack of gastric secretion. Undoubtedly the case would be placed in the achylia group, and yet pepsin, when properly activated, was found when tested. There is here once more a complete inhibition or delay of the psychical secretion to be followed by an appreciable secretion during the second stage of gastric digestion. The specimens in this case answered the description of wet achylia. After thorough irrigation and treatment of the stomach, perceptible free acid was found earlier in the digestive cycle.

(Note.—At present writing, some six months later, well; but incomplete return of secretion.)

Case VII.—Mrs. Gr. is a case in every way similar to the case described as Case VI. Empty stomach is negative, but in this young woman, who complains of discomfort and distress after eating, no actual pain shows the following findings after the administration of an Ewald meal:

Time.	Total acidity.	Free acid.	Pepsin.
5 mins.	4.0	0	0
10 “	4.0	0	0
15 “	5.0	0	0
30 “	7.0	Trace mucus	+
45 “	11.0	Trace mucus	+
1 hour	29.0	6.0 mucus	+
1¼ hours	30.0	Trace mucus	++
1½ “	6.0	mucus	
1¾ “			

Prolongation of digestion; still an appreciable rest after two hours; intimate mucus in all the specimens, indicating a well-marked catarrh; occult blood negative; starch digestion advanced; yeast, trace; lactic acid, slight trace; many bacteria indicating an infected mucosa; likewise vegetable debris, but no meat, there being atony and stagnation.

Spurious achylia, catarrh, atony, dilatation (?)

We have been able to demonstrate an experimentally induced achylia even in hypersecretory individuals by means of certain hypertonic solutions. The results of this work will appear shortly but it seems proper to state that both hypertonic salt solution and dextrose solutions are capable of inducing a definite delay in the appearance of gastric secretion for eighty minutes or more. This is of considerable interest inasmuch as water alone is capable in these subjects of giving rise to a perceptible secretion.

In conclusion we may state:

1. True achylia in which there is a total lack of acid and enzymes through the entire period of gastric digestion is exceedingly rare.

2. By means of the fractional method we have been able to study the entire period of gastric digestion in cases of achylia. On the basis of Pawlow's work, it is suggested that if his conception of gastric secretion be correct, it should follow that achylia can be either psychical or chemical. A total absence of secretion in the first hour of digestion, followed by a perceptible secretion in the second, would favor the belief that a psychical achylia (nervous) exists. The reverse, falling off in secretion, would favor the interpretation of a chemical achylia. A total lack of secretion through both phases might indicate a deficiency of both functions or an inactive mucosa.

3. Our studies show that the commonest form is a complete lack of gastric secretion through both phases (total achylia); two cases were encountered of true psychical achylia, but a pure chemical achylia was never encountered.

4. Attention is called to spurious achylia, which is quite common, and in which there is an ultimate elaboration of juice late in digestion, and always enzymes present.

5. By means of the administration of parathyroid extract in two cases of *bona fide* achylia, one of over ten years' duration, a perceptible return of the gastric secretion was noted during the psychical phase. Dietetic and local treatment were instituted at the same time.

6. The phase method of examination is of great value in determining the type of achylia as well as the possibility that at some phase the secretion might still be active, as shown in several of the cases recorded. This finding distinctly improves the prognosis.

ALTERNATION OF THE PULSE: A COMMON CLINICAL CONDITION.

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The purpose of the present communication is, in the first place, to express the frequency of pulsus alternans as a clinical condition, and, secondly, to report the analysis of histories, clinical findings, and cardiographic records of this series of cases. I have found alternation of the radial pulse in 71 patients in the wards and among the out-patients of the Massachusetts General Hospital during a period of eight months. Radial pulse tracings were taken from 300 cardiac and cardiorenal cases in all.

Pulsus alternans is that condition of the pulse in which strong and weak beats alternate, but in which the cardiac rhythm is normal. It includes constant alternation and alternation found in phases and after premature beats only. The pseudo-alternation due to the late appearance of premature beats and due to respiratory influences must be differentiated from the true alternation (Figs. 2, 3, 6, 7, 8, and 9).

The clinical literature on the subject includes reports of small numbers of cases, usually from one to four or five, with scarcely a hint that all around us alternation of the pulse lies undiscovered. Mackenzie[1] has seen the condition often during a considerable number of years, and now has records of "over 100 cases," collected during a decade or more. Windle,[2] in 1913, reported 45 cases collected during a period of over four years.

Gravier,[3] in 1914, published a thesis in which, at considerable length, he discusses the theories of alternation and the experimental work on the subject, and details a study of 40 cases which he had collected with the help of Gallavardin during the course of two years. I would refer to his extensive bibliography for the literature on the subject.

Neither Mackenzie, Windle, nor Gravier[4] express the frequency of alternation of the pulse. They indicate that it is not rare. It is the writer's aim to show that it is a common condition.

In the present communication the alternation found in the rapid pulses of auricular flutter (Figs. 1, 2, and 3) and paroxysmal tachycardia (Fig. 4) is not included.[5] Also, the pseudo-alternation due to respiratory blood-pressure changes (Figs. 5, 6, and 7) and to delayed appearance of premature beats (Fig. 8) is excluded. Doubtful cases of true alternans have been omitted. Of the 71 cases found, 15 showed a constant alternation, 55 a post-premature beat alternation only, and 1 a phasic alternation.

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[1] Diseases of the Heart, 1913, p. 260.

[2] Quart. Jour. Med., 1913, vi, 453.

[3] L'Alternance du Cœur, Etude Critique et Clinique, Paris, 1914.

[4] Gravier makes a prophecy on page 270 of his monograph "L'Alternance du Coeur" as follows: "Il ne fait donc pas de doute pour nous que le pouls alternant ne soit bientôt reconnu comme un *symptôme fréquent* de l'insuffisance cardiaque."

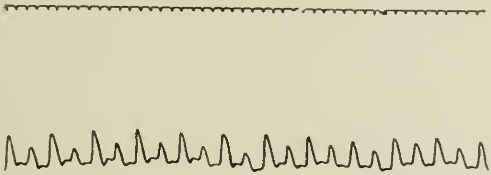

FIG. 1.—Pulsus alternans in a patient about two hours after the onset of an attack of auricular flutter. In tracings one hour and one and one-half hours after the onset of the flutter at the same rate as the present (144) no alternation occurred. Time interval = 0.2 second.

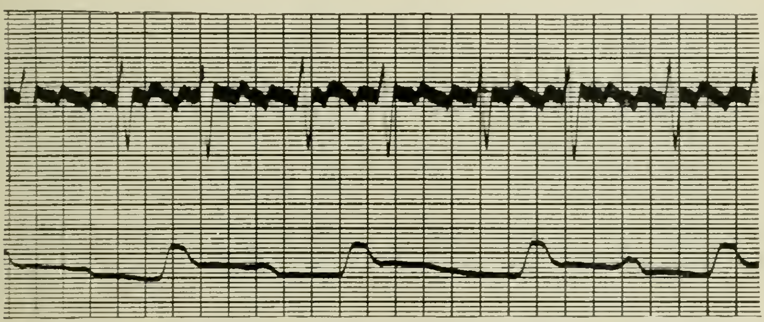

FIG. 2.—Pseudo-alternation from a case of auricular flutter. Simultaneous records of Lead II of the electrocardiogram above and radial pulse below. Abscissæ = 0.2 second. Ordinates = 10^{-4} volts.

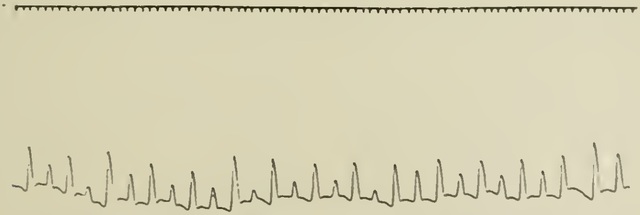

FIG. 3.—Radial tracing from patient whose record is shown in Fig. 2. Pseudo-alternation of auricular flutter. Time interval = 0.2 second.

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[5] During the eight months, three patients showing flutter and one showing paroxysmal tachycardia had alternation, the latter displaying the condition only at a rate of 185 and not at the lower paroxysmal rates of 150 and 100, or at the normal rate of 60, a fact which reveals the exhaustion rate of this heart.

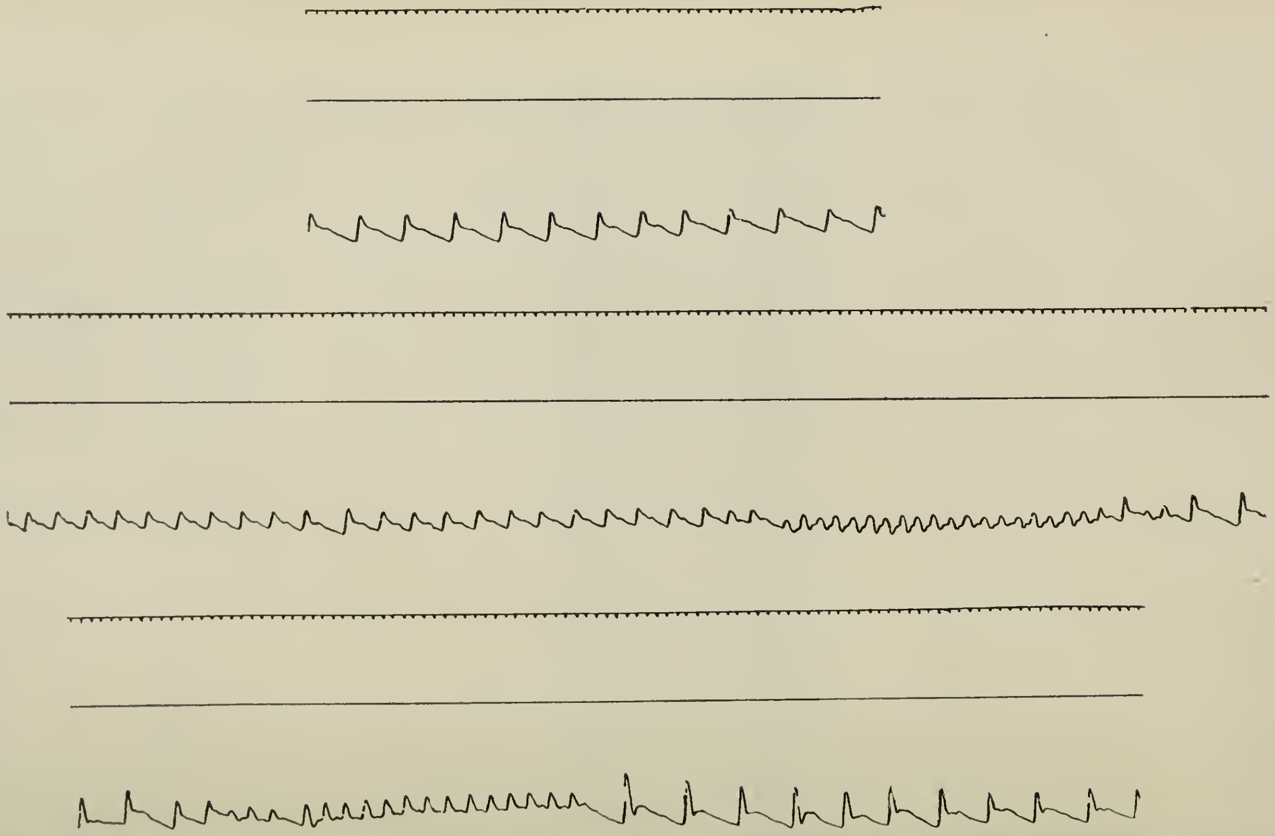

FIG. 4.—Radial tracing from a patient, showing three rates of paroxysmal tachycardia. Interval of a few seconds between strips of tracing. Upper tracing shows the normal rate (60); middle tracing shows two rates of tachycardia (first 100, second 185); lower tracing shows a short paroxysm at a rate of 150, with return to the normal rate of 60. Alternation is present in the pulse at the highest

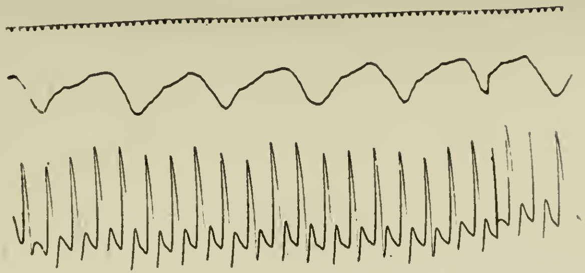

Fig. 5.—Simultaneous respiratory and radial tracings, showing well the respiratory change in the force of the pulse. In this instance pulsus paradoxus is present. In the respiratory record the rise of the curve represents expiration and the descent inspiration. Respiratory rate is 25, pulse rate 92 per minute. Time interval = 0.2 second.

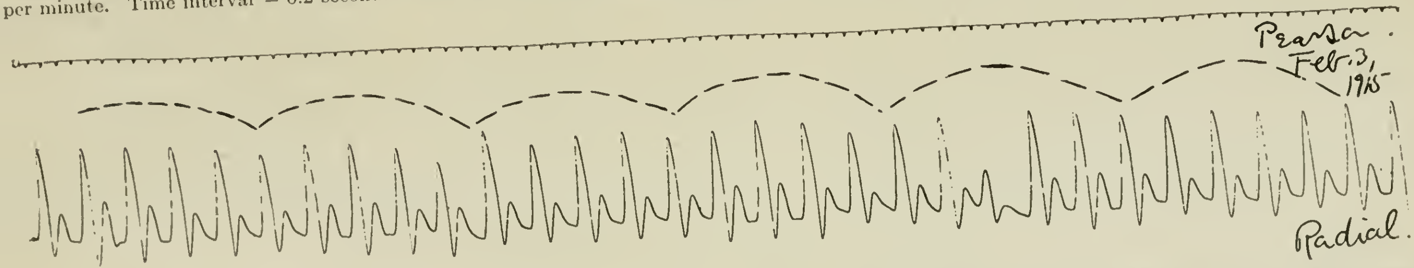

Fig. 6.—Pseudo-alternation following first premature beat. No alternation after second premature beat. Line of dashes represents the respiratory changes in the pulse volume. The first premature beat is followed by a natural rise in the volume while the second premature beat is followed by a drop. Hence the alternating beat after the first premature beat is due to respiratory and not myocardial conditions. Time interval = 0.2 second.

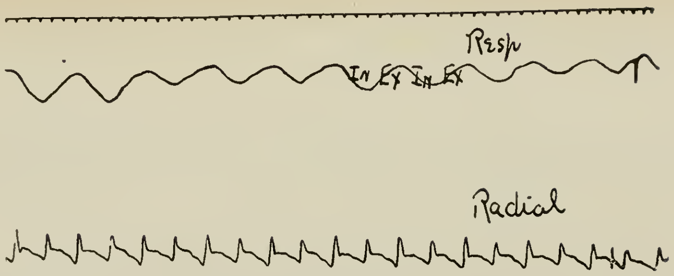

FIG. 7.—Simultaneous respiratory and radial tracings. Respiratory rate is 55 and pulse rate 110 to the minute. The alternation is due here to this exact relationship, and is not a true alternation. Downstroke in respiratory curve represents inspiration, upstroke expiration. Time interval = 0.2 second.

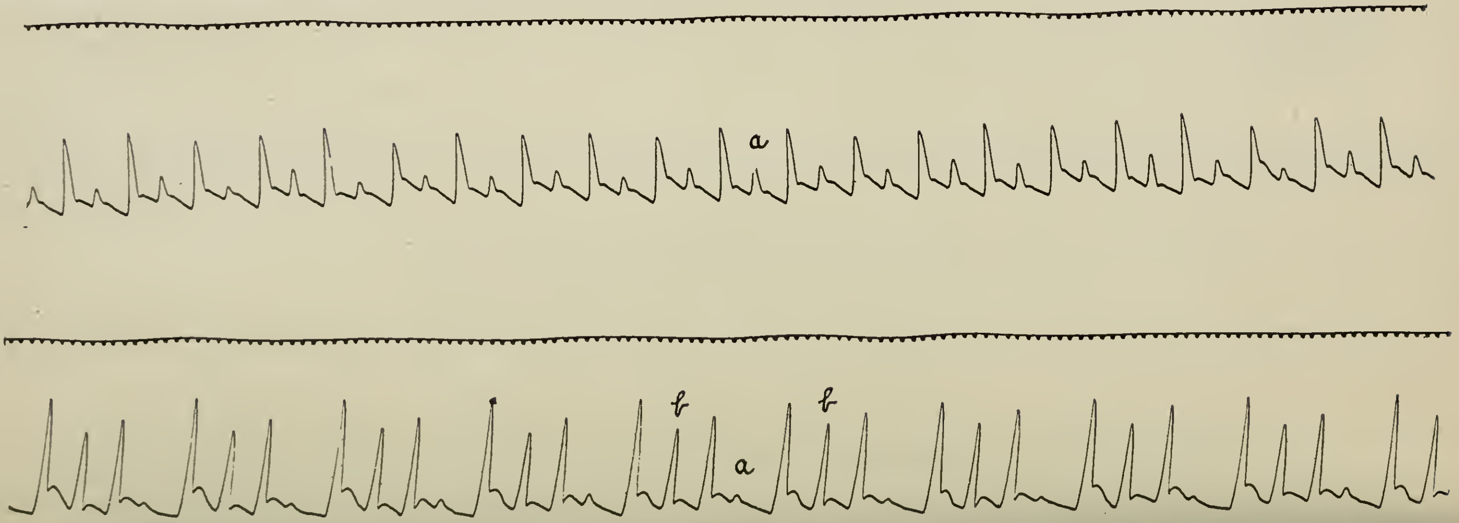

FIG. 8.—Radial tracings from same patient a few seconds apart, the upper one showing a pseudo-alternation due to bigeminy from ventricular premature following a ventricular premature beat which falls every fourth beat. *a* = ventricular premature beat.

The findings by months has been quite uniform, 8 to 10 being the usual figure. From August 1, 1914, to November 30, 1914 inclusive 33 cases were found, and from December 1, 1914, to March 31, 1915 inclusive 38 more were discovered, making a total of 71 for the eight months. On the two medical services of 40 to 50 beds each, 51 patients were found to have pulsus alternans, 18 out-patients showed the condition, and 2 cases were found in the surgical wards. The medical services received the closest observation, although in these undoubtedly a few cases slipped by unrecognized and untraced. Among the out-patients and in the surgical wards relatively little time was spent. During two recent months in the out-patient department of the hospital, Dr. J. H. Pratt and four medical students limited their attention entirely to cardiac cases, and found among them 6 cases of alternation (8 per cent. of 74 from whom radial tracings were taken).[6] This fact indicates that during eight months in which I studied the condition, probably less than half of the out-patient alternations were missed.

The frequency of alternation as compared with other abnormalities of the heart beat found by me at the Massachusetts General Hospital in eight months may best be shown in tabular form:

Table I.

Ventricular premature beats	119	cases
Pulsus alternans	71	"
Auricular fibrillation	71	"
Auricular premature beats	22	"
Defective *A–V* conduction and block, including twelve bundle branch lesions (long *As–Vs* interval not preceded by digitalis administration)	21	"
Paroxysmal tachycardia	9	"
Auricular flutter	6	"

Alternation of the pulse was found in 33 per cent. of all cases showing any degree of cardiac decompensation from whom a radial pulse tracing was obtained. Table II shows the relative frequency of the various abnormalities of the heart beat in decompensation.

Table II.

Cases of cardiac decompensation traced in eight months	201	
Pulsus alternans	66	(33 per cent.)
Auricular fibrillation	65	(32 per cent.)
Normal pulse	24	(12 per cent.)
Ventricular premature beats without alternation	20	(10 per cent.)
Defective conduction without alternation following digitalis	12	
Defective condition with and without alternation following digitalis	19	
Defective conduction without alternation not following digitalis	8	
Defective conduction with and without alternation not following digitalis	20	
Auricular premature beats without alternation	4	
Auricular premature beats with and without alternation	8	
Auricular flutter	2	

[6] The writer is indebted to Dr. Pratt for these figures.

Seventy-two cases of non-fibrillating hearts showing hypertension (systolic blood-pressure constantly above 160 mm. of mercury) were examined, and of these 37, or *51 per cent.*, showed alternation. The association of alternation and hypertension has been pointed out by Windle,[7] Gravier,[8] Lewis,[9] and others, and among the cases reported in the literature, hypertension occurred in a large percentage.

The relationship of age to pulsus alternans in the 71 cases is shown in Table III.

TABLE III.

Years of age.		Number of cases of pulsus alternans.
0 to 10	0	11 (15 per cent.) below the age of forty.
10 to 20	2	
20 to 30	2	
30 to 40	7	
40 to 50	16	
50 to 60	17	44 (62 per cent.) above the age of fifty.
60 to 70	17	
Over 70	10	

The youngest patient was fifteen years of age[10] and the oldest seventy-five years. The majority of Windle's patients were old arteriosclerotic people.

SEX. Of the writer's series 49 (69 per cent.) were male and 22 (31 per cent.) female.

In the attempt to determine the etiological factors of the cardiac condition the following data have been obtained:

TABLE IV.

Clear history of rheumatism, chorea, or tonsillitis	9	cases	(13 per cent.)
Clear history of syphilis	4	"	(6 per cent.)
Wassermann test positive (of 60 cases tested)	9	"	(15 per cent.)
Hypertension: systolic pressure constantly above 200 mm. mercury	12	"	(17 per cent.)
total constantly above 160 mm. mercury	37	"	(52 per cent.)
diastolic pressure (of 68 cases tested) above 100 mm. mercury	32	"	(47 per cent.)
Age, patients over fifty years[11]	44	"	(62 per cent.)
Excessive alcohol	13	"	
Excessive tobacco	12	"	
Excessive tea or coffee	11	"	

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[7] Loc. cit. [8] Loc. cit. [9] Clinical Disorders of the Heart Beat, 1914, p. 104.

[10] A few days after the expiration of the eight months a girl, aged ten years, was discovered to have true alternation of the pulse.

[11] The relationship of the arteriosclerosis of old age and pulsus alternans has been studied by tracing the radial pulse of 69 patients at the Massachusetts State Hospital at Tewksbury and at the Long Island Hospital, City of Boston. Among these arteriosclerotic people, nearly all over sixty years of age, but few presented much evidence of cardiac decompensation, 5 showed alternation of the pulse, 4 in but slight degree after premature beats, 16 showed auricular fibrillation, 14 ventricular premature beats, 5 auricular premature beats, and 2 defective *A–V* conduction. The oldest patient, aged ninety-seven years, showed ventricular premature beats but no pulsus alternans; she looked as though she might readily live to be ten years older in spite of her marked peripheral arteriosclerosis. I am indebted to the resident physicians of the hospitals at Tewksbury and Long Island for the opportunity to examine their patients.

The severe acute infections are probably infrequently attended by alternation of the pulse. Of 10 severe cases of pneumonia and 4 of typhoid only 1 (typhoid fever with defective heart) showed alternation.

Digitalis played no part whatsoever in the etiology of alternation in more than half of the cases, for 40 patients had received none so far as I was able to determine prior to the pulse tracing. The failure to find alternation in the pulse of two typhoid patients who had a considerable degree of heart-block from digitalis or in that of two surgical cases in whom a postoperative digitalis blocking was produced (in one of these a prolonged *a–c* interval was found with a pulse rate of 105), suggest that digitalis may have played no role in the causation of the alternation in the other 31 cases of the series.

The relationship of clinical conditions such as angina pectoris to alternation has also been of interest. The present large series of cases affords useful data.

Table V.—Clinical Conditions Associated with the Alternation of the Pulse.

Dyspnea (constant or on slight to moderate exertion)	66	cases	(93 per cent.)	
Dyspnea without physical signs of decompensation	28	"	(39 per cent.)	
Dyspnea with very marked physical signs of decompensation	9	"	(13 per cent.)	
Angina pectoris	6	"	(8 per cent.)	
Cheyne-Stokes breathing	6	"	(8 per cent.)	
Albuminuric retinitis (18 fundi examined)	8	"		
Albuminuria	45	"		
Glycosuria	3	"		
Valve lesions—Mitral stenosis alone	3	"		Total, 15 cases 21 per cent.
Aortic valve lesion alone	4	"		
Aortic and mitral	5	"		
Mitral regurgitation alone	3	"		

Hypertrophy of the heart was usually found on physical examination and 24 cases which were examined with the Roentgen-ray (the patient's chest seven feet from the tube) showed definite cardiac enlargement in every instance. The great vessels were abnormally wide in 5 of the 24 cases.

Findings by Graphic Methods.—The pulse of each case was examined with the Mackenzie ink polygraph and 44 of the 71 cases were also electrocardiographed. The following two tables show the analyses of the records made.

TABLE VI.—POLYGRAPHIC RECORDS.

Constant alteration (Fig. 9)	15 cases	(21 per cent.)
Alternation after premature beats only	55 “	(77.5 per cent)
Alternation after premature beats only (marked) (Fig. 10)	15 “	(21 per cent.)
Alternation after premature beats only (slight) (Fig. 11)	40 “	(56.5 per cent.)
Phasic alternation	1 case	
Ventricular premature beats	67 cases	(94 per cent.)
Auricular premature beats (3 with v.p.bs.)	4 “	(6 per cent.
No premature beats	3 “	(4 per cent.)
Defective $A-V$ conduction (two after digitalis)	3 “	
Paroxysmal tachycardia at other times	2 “	
Pulse rate at time of alternation:		
Under 100 per minute	53 “	(75 per cent.)
Lowest rate, 57; highest rate, 125.		

TABLE VII.—ELECTROCARDIOGRAPHIC RECORDS (44 OF THE 71 CASES WERE ELECTROCARDIOGRAPHED).

Evidence of lesion of right branch of $A-V$ bundle	7 cases	(16 per cent.)
Evidence of lesion of left branch of $A-V$ bundle	0 “	
Evidence of defective $A-V$ conduction (long $P-R$ interval) not after administration of digitalis	5 “	(11 per cent.)
Other cases with long $P-R$ interval after administration of digitalis	7 “	
Aberrant ventricular complexes (other than bundle branch lesion)	3 “	
Total of cases evidencing damage to conducting system (including one discovered with the polygraph)	15 “	(34 per cent.)
Left ventricular preponderance	22 “	
Right ventricular preponderance	3 “	

The T deflection was flat or inverted in 13 and low in 2 of 24 cases who had not been taking digitalis.

Eighteen of the 44 electrocardiograms showed premature beats, and in 7 of these cases there was slight alternation of the T deflections afterward (Figs. 12 and 13), in 6 in accord with the radial alternation and in one in reverse order. In 3 cases there was slight alternation of the $R-S$ deflections after premature beats. No constant alternation of the $R-S$ or T deflections occurred. There was no alternation of the P complexes found.

Sinus arrhythmia was a frequent finding.

TABLE VIII.—SINUS ARRHYTHMIA ASSOCIATED WITH ALTERNATION OF THE PULSE.

Marked	6 cases	(8 per cent.)
Moderate	20 “	(28 per cent.)
Slight	16 “	(23 per cent.)
None	20 “	(28 per cent.)
Questionable	9 “	(13 per cent.)

The small percentage of marked sinus arrhythmia occurring with the alternation is probably accounted for by the relatively old age of the majority of the patients, but the frequency with which some degree of sinus arrhythmia occurred with pulsus alternans in the

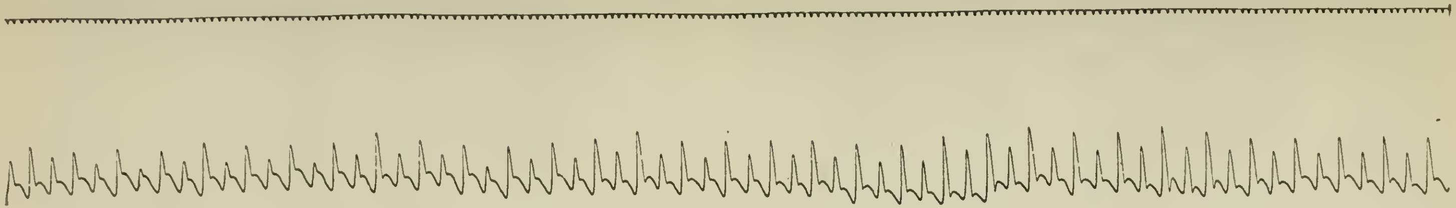

FIG. 9.—Constant pulsus alternans. Rate 102 per minute. Time interval = 0.2 second.

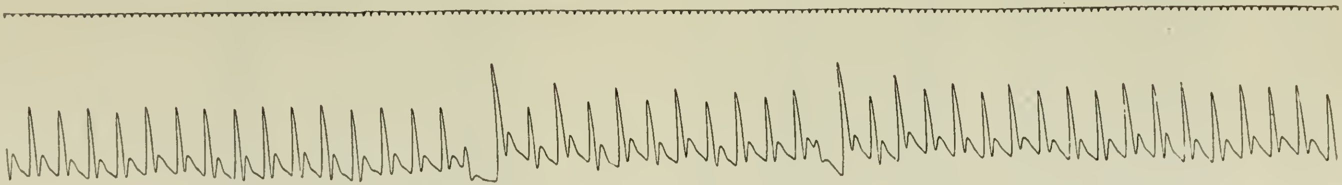

FIG. 10.—Marked postpremature beat alternation. Rate 84 per minute. Time interval = 0.2 second.

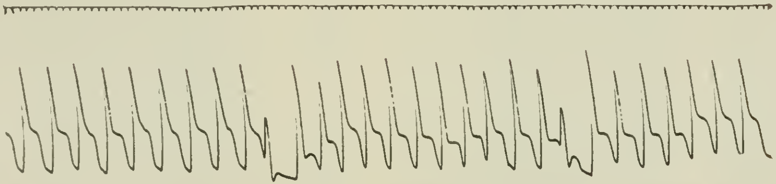

FIG. 11.—Slight post-premature beat alternation. Rate 87 per minute. Time interval = 0.2 second.

present series is a noteworthy fact. The response of the heart to nervous impulses may be active, although the cardiac contracting power is much diminished.

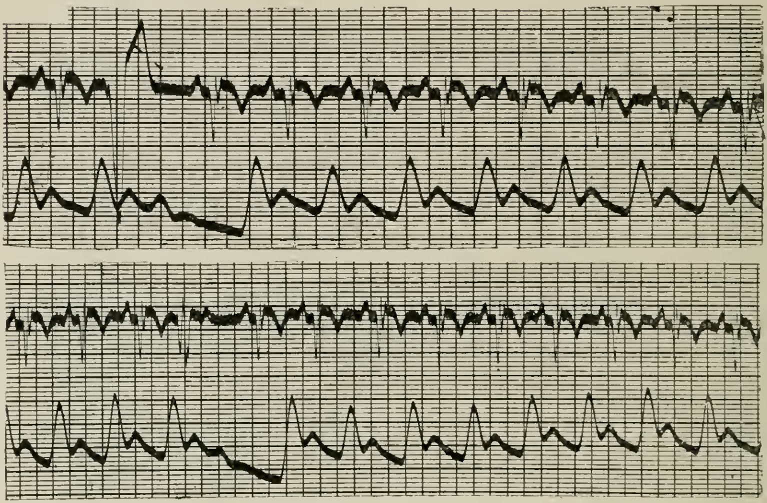

FIG. 12.—Simultaneous records of electrocardiographic Lead II and radial pulse of patient, showing slight post-premature beat alternation. Note slight alternation of the *T* deflections after the premature beats. Time interval = 0.2 second.

THERAPY. Digitalis was given to 53 of the 71 cases and clinical improvement followed in 32 cases (60 per cent.), illustrating well

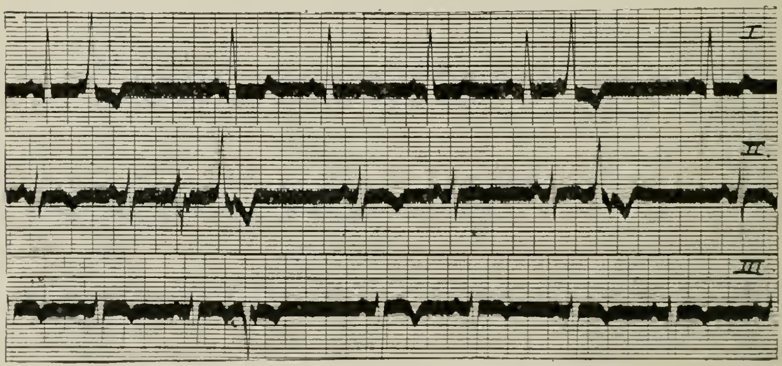

FIG. 13.—Leads I, II, and III of patient who showed slight alternation of the radial pulse after ventricular premature beats. Note post-premature beat alternation of the *T* deflections. Left ventricular preponderance is shown by Leads I and III. Abscissæ represent fifths of a second, ordinates represent 10^{-4} volts.

the fallacy of the old-time belief that it is unwise to give digitalis to an alternating heart. In 4 cases the degree of alternation was lessened after digitalis, in others judgment could not be passed because premature beats which had appeared and had been followed by alternation no longer occurred after the administration of digitalis.

PROGNOSIS. One of the most important relationships of alternation is that to prognosis. Since but a very short interval has elapsed since the eight months during which the cases here recorded were collected, it is impossible to give more than a suggestion as to the prognostic significance of the pulsus alternans. Twenty-two of the cases (31 per cent.) are known to have died during the eight months, most of them a few months after the condition was discovered. During the ninth and tenth months three more are known to have died, making a total to date (June 1, 1915) of 25 deaths (35 per cent.). Of the 25, one patient is known to have had pneumonia at the time of death, another streptococcus septicemia, a third malignant disease of the liver, and a fourth was comatose following a cerebral hemorrhage. Two of the 25 were below the age of forty years (the younger being fifteen years old) and 13 were over fifty years old; 10 had visited the out-patient department of the hospital within a few months or a few weeks before death; that is, they were ambulatory patients at the time their alternation was in progress.

The relationship of the degree of alternation to prognosis is shown in the following table:

TABLE IX.

	Number.	Dead.	Percentage.
Cases showing constant alternation	15	8	53
Cases showing marked post p. b. alternation . .	15	7	47
Cases showing slight post p. b. alternation . .	40	10	25

Tabora[12] has spoken of a case of pulsus alternans alive six years after the condition was found; this is the longest survival on record.

Pathological Findings. Of 6 cases dying at the Massachusetts General Hospital, 3 came to autopsy. All 3 showed coronary sclerosis in some degree, and 2 also showed on gross examination of the endocardium areas of fibrosis; 1 case showed marked sclerosis of the aorta.

The weights of the three hearts were high—384 grams, 403 grams, and 475 grams respectively.

Microscopic examination of the kidneys showed in all an arteriosclerotic nephritis.

VALUE OF METHODS OF DETERMINING ALTERNATION. A graphic record of the pulse is the only satisfactory method in searching for alternation, and even then one must be prepared to take a record of considerable length. This can be done well with an ink sphygmograph, long rolls of paper being available at very little expense and effort.

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[12] Conversation with Gravier, "L'Alternance du Cœur," p. 282.

Palpation of the radial pulse revealed the alternation in 13 of the 15 cases showing the condition constantly. It was also felt in several of the cases of post-premature beat alternation, but this finding is very unreliable, because of the impossibility to detect the difference by the finger between very late premature beats (as in a bigeminal pulse) and weak alternating beats. This criticism applies also to Gravier's delicate bimanual method. Rarely this difficulty may also be experienced in the radial tracing itself on measurement. In such instances a simultaneous jugular tracing or, better still, an electrocardiogram will settle the matter.

Auscultation of the heart is notoriously unreliable. Kahn[13] has published experimental phonocardiograms showing the alternation in intensity of the heart sounds in dogs whose hearts were alternating; but when one listens to the hearts of patients whose radial pulse alternates, the difference in intensity of the sounds is slight at the most. In one case of the 71 recorded here who showed very marked constant pulsus alternans, the heart sounds varied not at all in intensity.

Rehberg's test,[14] which consists of the finding of a difference in the blood-pressure of alternating beats is cumbersome but reliable if a graphic record is taken; the auscultatory method in the use of the blood-pressure cuff is unsafe on account of the inaccuracy of auditory measurement in distinguishing between late premature beats and alternation.

Delay in the Appearance of the Small Alternating Beat at the Wrist. This delay was pointed out in the first description of pulsus alternans by Traube[15] himself in 1872, and has been frequently found since. Of the 15 constant alternations in the present series, 6 showed well this delay, 5 showed it slightly, and 4 failed to show any measurable delay. An analysis of 25 post-premature beat alternations shows a simple delay of the small beat or beats in 12 without apparent shortening of the *As–Vs* interval after the premature beat. In 5 cases the *As–Vs* interval after the premature beat was shortened, and in 7 cases there was a combination of this shortening with the usual alternation delay, thus magnifying the delay of the first weak alternating beat (Fig. 14). Sinus arrhythmia sometimes confused the picture slightly, but the curves were studied which showed none or very little.

Other Observations. The relationship of the prematurity of the forced beats to the degree of alternation is seen, as a rule, only in comparison of early beats with those coming so late that they occur almost at the normal point after the preceding beat (Fig. 15). In such cases the alternation is greater after the more premature beat, a condition that would be expected on account of the

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[13] Arch. f. d. ges. Physiol., 1911, cxl, 471.

[14] Ztschr. f. klin. Med., Berlin, 1909, lxviii, 247.

[15] Berl. klin. Wchnschr., 1872, ix.

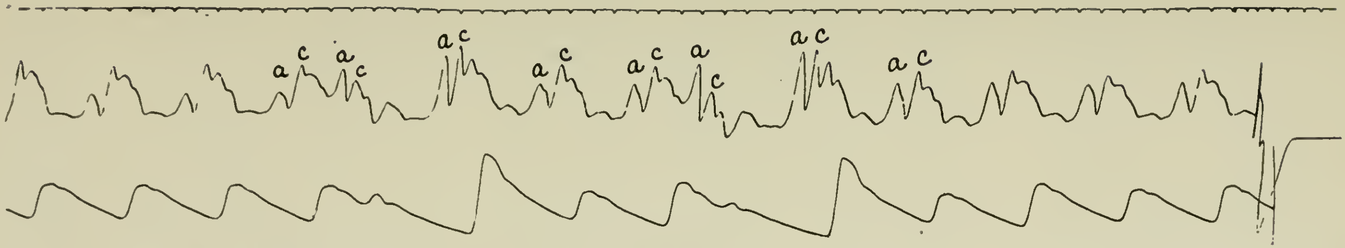

Fig. 14.—Polygram from patient exhibiting slight post-premature beat alternation. The upper record is of the jugular pulse, the lower of the radial pulse. Two auricular premature beats are shown. The *a–c* interval following each premature beat is shortened. Time interval = 0.2 second.

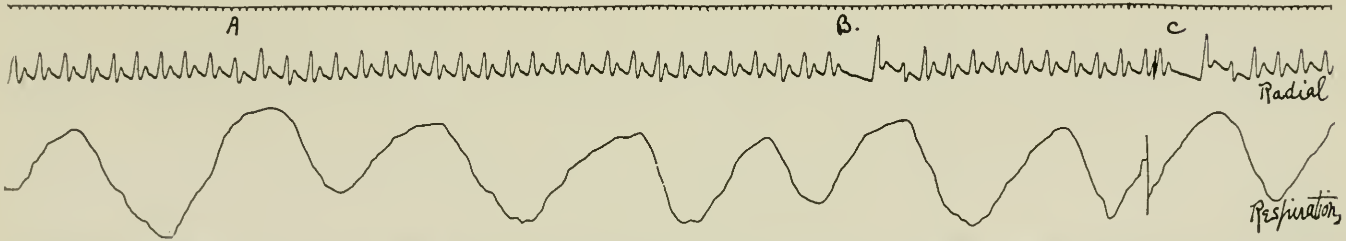

Fig. 15.—Simultaneous respiratory and radial tracings from a patient exhibiting post-premature beat alternation. In the respiratory curve the rise represents expiration and the descent inspiration. The late premature beat at *A* is followed by much less alternation than the early premature beats at *B* and *C*. Time interval = 0.2 second.

greater burden on the heart with the early beat. The alternation preceding premature beats as described by Windle[16] has been seen by the writer only in a patient who, while showing waves of increase and decrease of a constant alternation, happened to have a premature beat soon after the increase had begun. The sixth radial upstroke in Fig. 7 of Windle's paper may represent a late premature beat, thus explaining the alternation following.[17]

The relation of respiration and degree of post-premature beat alternation has been found to consist of a slight increase during inspiration and a slight decrease during expiration with ordinary breathing; with the pulsus paradoxus of thoracic respiration the reverse might be expected.

Summary. True alternation of the radial pulse has been found in 71 of 300 cardiac and cardiorenal patients examined with the sphygmograph by the writer at the Massachusetts General Hospital in the course of eight months (August 1, 1914, to April 1, 1915).

It has occurred as commonly as auricular fibrillation;[18] 66 of 201 cases examined who were suffering from cardiac decompensation in some degree showed pulsus alternans; 65 others of the 201 showed auricular fibrillation; 15 of the patients having alternation showed it constantly, 55 after premature beats only and 1 showed a phasic type. The finding of ventricular premature beats has been of considerable value in the present series, 77 per cent. of the cases requiring the premature beats before the alternation of the pulse was exposed.

The condition was found most often in people in late middle life or in old age. Hypertension was associated with the alternation in 52 per cent. of the cases. Cardiac enlargement was practically a constant finding. Syphilis and rheumatism apparently played a less important part in the production of the myocardial weakness than did arteriosclerosis.

Electrocardiographic examination of 44 of the cases gave evidence of damage to the *A–V* conducting system in 15 cases, or 34 per cent. Electrocardiographic alternation was found in the *T* deflections after premature beats in 7 of 18 cases which showed premature beats on the records obtained. Only in 3 cases was there any alternation of the *R–S* deflection after premature beats.

Sinus arrhythmia occurred frequently in the series.

Digitalis and rest in bed produced clinical improvement in 32 of 53 cases in which digitalis was administered even though the pulsus alternans may have persisted. In 4 cases the alternation was diminished or banished after this therapy.

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[16] Heart, 1910, ii, 95.

[17] Gravier has made this same observation concerning Windle's tracing, "L'Alternance du Coeur," p. 151.

[18] In 1906 A. Hoffman (Münch. med. Wchnschr., 1906, liii), wrote of finding 10 cases of complete arrhythmia and 10 cases of alternation of the pulse out of 183 cases traced.

Twenty-five of the 71 cases died within ten months from the beginning of this study, the majority of the deaths so far as could be determined attributable to the cardiac condition directly. The relationship of the degree of alternation to prognosis was as one would anticipate, the greater the degree the shorter the life after the pulse discovery.

Arteriosclerosis of heart and kidneys was found in the only three cases examined postmortem.

It gives the writer pleasure to acknowledge his indebtedness to members of the hospital staff for their coöperation.

MODE OF ACTION AND USE OF EMETIN IN ENTAMEBIASIS.

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The value of emetin in amebic dysentery is so well established that the further report of cases successfully treated would scarcely be of general interest at the present time. The literature on the subject is rapidly becoming voluminous, but the present status of the drug in the treatment of amebiasis has been excellently summed up in a rather recent paper by Vedder.[1] During the past eight months still further facts have come to light, so that the present communication will be limited to a practical discussion of the advances made in our knowledge concerning the mode of action of the drug, best methods of administration, dosage, ill effects, relapses, and other points of interest. In considering the mode of action of emetin in entamebiasis it will be necessary to inquire somewhat briefly into the habits and habitat of amebas in the body, and while some of the views expressed may be later proved incorrect, they at least permit of a rational basis for therapy.

Mode of Action of Emetin and Ipecac in Entamebiasis. The exact manner of action of ipecac and emetin in amebic disease was until a few years ago very indefinite. In the old days of ipecac therapy there were many theories but few facts. It can be stated now from experimental and clinical evidence that emetin is the active principle of ipecac from the amebecidal point of view. In 1912 Rogers[2] by the subcutaneous and intravenous use of emetin demonstrated that it owes its action chiefly at least to absorption into the blood stream with resultant destruction of the amebas in the tissues. It matters not whether the amebas be in the tissues of the colon, liver, or gums of the mouth.

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[1] Origin and Present Status of the Emetin Treatment of Amebic Dysentery, Jour. Amer. Med. Assoc., 1914, lxii, 501.

[2] Rapid Cure of Amebic Dysentery and Hepatitis by Hypodermic Injections of Soluble Salts of Emetin, British Med. Jour., June 22, 1912, p. 1424.

The question arises, Has emetin or ipecac any effect upon amebas not in the tissues or within reach of the circulation but in the lumen of the large intestines? Carter[3] believes that in giving the whole drug (ipecac in salol-coated pills) by mouth and emetin by needle that by the former method we insure that the intestinal contents are thoroughly permeated with the drug and in the latter we reinforce the amebecidal effect of the parent drug upon the parasites buried in the wall of the affected intestines by the hypodermic injections of emetin carried to them by the blood stream. He is convinced that acute amebic dysentery requires the entire root with all its alkaloids as well as emetin. If we accept these statements as true, undoubtedly our new treatment with emetin injections must be modified or rather complicated by the simultaneous oral use of large doses of ipecac. In short, we must return to the old, cumbersome ipecac therapy plus our emetin by needle. Do the facts justify the assertion that by giving ipecac orally we can thoroughly permeate the intestinal contents with the drug? In order to answer this question satisfactorily it is essential to know how ipecac or its active principles are eliminated from the body. Unfortunately all the text-books on modern pharmacology to which I have had access are uniformly silent upon this point. In hope of throwing a little light upon this subject the following investigation was made in 1912.[4] Stools from patients receiving ipecac in which no amebas had been found for at least two or three days were collected, filtered, and the filtrate sterilized by heat. The sterile fecal filtrates were added to growths of amebas *in vitro* and allowed to remain in contact for varying lengths of time. The result was that the amebas remained practically unaffected, showing that the feces contained none at least of the amebecidal constituents of the ipecac. This is the only experimental evidence I am aware of against the elimination by the large bowel of the amebicidal principles of ipecac (chiefly emetin). The experiment, however, still lacks confirmation. Furthermore, it has been demonstrated *in vitro* that emetin (also ipecac) is highly destructive to practically all species of amebas. Even clinically, evidence[5] has recently come to light showing the specificity of emetin on a species of amebas found in the alveolar tissues in Rigg's disease.

There exists in the intestines of many normal individuals the harmless *Entameba coli*. This organism should be easily destroyed by emetin (or ipecac) if the drug is eliminated by way of the intestines. The following case will prove of interest in this connection:

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[3] Emetin and Ipecacuanha: Their Amebecidal Value in Pathogenic Amebiasis, Indian Med. Gaz., March, 1914.

[4] Observations on the Effect of Ipecac, Phenol, and Salicylic Acid in Vitro, New Orleans Med. and Surg. Jour., 1912, lxiv, 884.

[5] Protozoa of the Mouth in Relation to Pyorrhea Alveolaris, Dental Cosmos, 1914, lvi, 948.

In 1913 I had occasion to treat a physician of this city for a chronic diarrhea. He had contracted amebic dysentery in Cuba seven years previously. Two years later he took a thorough course of ipecac, but a moderate diarrhea still continued. In 1912 a sigmoidoscopic examination revealed nothing abnormal. When seen by me in November, 1913, he was having a few loose stools early in the morning, but later the passages would become solid. The stools showed fermentation and were not dysenteric in character. Microscopically there was no blood or pus but some mucus, trichomonads, and also what appeared to me to be typical *Entambœ coli*. Because of the patient's suspicious past history he was given therapeutic test with emetin. One grain of the hydrochlorid was injected daily for seven days. At the end of this period there was no improvement. Examination of the stool still showed vegetative entamebas (small, granular, sluggishly motile amebas, with well-defined nuclei). Under diet, rest, and attention to kidneys the patient was markedly improved.

The result of this case adds further weight to the contention that emetin is not eliminated from the blood stream by way of the alimentary tract otherwise the *Entamebœ coli,* which are simply harbored in the intestines should have been readily destroyed. The non-pathogenicity of the colon entameba is due in all probability to the fact that it does not penetrate the intestinal mucosa. This explains why neither ipecac nor emetin, orally or by needle, has any effect upon them. By analogy the pathogenic entamebas which are free in the intestinal canal should remain unaffected by our specific medication and cause no symptoms. Such is found to be the case in the carrier state. Finally, the amebicidal action of ipecac and emetin is limited then to the amebas in the tissues. When these are all destroyed the lesions heal with remarkable rapidity and the patient is cured.

Relapses and Carriers. Unfortunately in a certain proportion of cases we find that relapses occur or the patient remains well, but his stools still contain the pathogenic entamebas and the individual becomes a carrier. Just why a relapse occurs in one case and the carrier state in another cannot be explained satisfactorily at present. Naturally both conditions depend upon the survival of some of the entamebas.

To enter into a slightly more detailed discussion of this subject might appear, at first sight, to be only of theoretical interest, but it will be found, when we come to therapy, to be of considerable practical value, as we do not treat the two conditions alike.

Relapses, in most instances, are due to the fact that some of the amebas escape destruction by encystment. In this stage they are resistive to any form of medication and produce little, or at times, no local irritation. From careful history taking in some 80 cases of amebic dysentery I have found that in the majority of instances it will be noted that even in periods of improvement or apparent well-being the patient will usually admit that he experiences some slight abdominal discomfort or unnatural feeling in spite of the fact that the stools were apparently normal. From this I am strongly inclined to believe that in the majority of cases some of the cysts remain imbedded in the tissues of the colon and are not simply harbored in the large intestine in the same manner as the *Entamebæ coli*. For if such were the case there should be complete absence of symptoms in the intervals of remission. The relapse takes place then when conditions are favorable for the encysted forms to again become vegetative.

In the carrier state it would appear however, that conditions are somewhat different. Here the individual who is a menace[6] to the community is himself apparently immune to the organism which simply lives in his intestines. What it is that protects the intestinal mucosa in such a case from penetration by the parasite is not known, but this fact constitutes the essential difference between the two states.

Modes of Administration. There are at the present time four routes by which emetin has been introduced into the body: the subcutaneous, the intravenous, the oral, and the rectal. It is important for effective therapy to know the advantages and disadvantages of each method. In the following discussion the hydrochloride of emetin will only be considered, with occasional reference to ipecac.

The Subcutaneous and Intravenous Routes. For practical purposes these two methods of administration may be considered together. The intravenous route is only necessary in exceptional cases and does not differ from other intravenous medication.

With regard to the subcutaneous injections of the drug there are several facts to be borne in mind: (1) that the alkaloid emetin is slightly irritating, and (2) the hydrochloride is slightly acid in reaction (the degree of acidity varies somewhat in preparations from different pharmaceutical houses). Where a small dose is injected, such as one-third grain, both of these factors are negligible, as the product is rapidly absorbed into the circulation. On the other hand if a large dose is administered (as one grain) considerable local pain and inflammation results, owing to the concentration of the factors just mentioned. Intramuscular injections cause still more discomfort. The inflammatory reaction thus produced at the site of inoculation may persist as an infiltrated area for from one to two weeks. It is more than probable that such a reaction seriously retards the rapid absorption of the drug.

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[6] Walker and Sellards, Experimental Entamebic Dysentery, Philip. Jour. Sci., 1913, Sec. B., No. 4, 253.

For these reasons where prompt and lasting effect is desired, small repeated injections are far preferable to large single doses.

Oral Route. When emetin is administered by mouth it is highly probable, from what has been previously stated, that the drug is absorbed into the blood stream in the small intestines and is not eliminated by way of the colon in the fecal matter. The drug is usually taken in salol or keratin-coated pills:

My first experience with this method occurred in April, 1913, in a man aged forty-four years, with a severe dysentery and hepatitis. Because of the urgency of the symptoms (fever, abdominal pain, large tender liver, and leukocytosis) it seemed important to get the patient rapidly under the influence of the drug. He was accordingly given one-third grain of emetin hydrochloride by needle and by mouth, twice a day, that is, a total of one and one-third grains daily. The emetin was put up in one-third grain salol-coated pills. Ignorant of the contents of the pills the patient thought from the effect that he was taking a drastic purgative. There was considerable abdominal discomfort and a marked increase in the number of stools. After two days it was necessary to stop the drug by mouth and improvement rapidly ensued.

This irritant action of emetin when taken by mouth is well exemplified in a case I was called in to see by Dr. Matas through whose courtesy I am reporting it. The circumstances are briefly as follows:

The patient was a white male, Italian, aged seventy years. Admitted to the Charity Hospital in November, 1913. The disease began one month previous to admission with a bloody diarrhea. The diagnosis of hepatic abscess was made and the patient was operated upon by Dr. Matas. Two days after the operation the patient was put on emetin, and given one grain by needle daily. In less than two weeks he was entirely free from temperature. The patient then refused further injections of emetin because of the soreness of his arms. Thereupon it was decided to continue the emetin by mouth in the same dosage, the ampoules being simply emptied into water. This solution caused no vomiting but his stools began to increase in number. Ten days later, when I was asked to see him, his bowels were extremely loose and he was very emaciated and feeble. Examination of the stools failed to show amebas but there were blood clots, pus, and mucus present. Recalling my first experience with the oral method I advised simply discontinuing the emetin. The patient made a slow but uneventful recovery. When seen two months later he had had no further return of his amebic affection.

Here we have the curious spectacle of a man being cured and killed by the same drug. Undoubtedly the administration of emetin was prolonged unnecessarily. Another surprising fact was the ability of the patient to retain large doses (one grain) of the drug by mouth.

In order to determine the amount of gastric and intestinal irritation produced by the oral ingestion of smaller doses, the writer took a half-grain of the same preparation of emetin in solution. This caused nausea and vomiting after an interval of an hour. This was followed in another hour by two loose stools accompanied by griping, and some abdominal discomfort persisted for five or six hours. After this experience, in order to avoid the psychic element, I gave one-half grain by mouth to an unsuspecting, healthy young negro. He suffered no nausea, but one hour and a half later he had two watery passages with considerable abdominal discomfort.

Low[7] reports good results in two cases of amebic dysentery in which he used keratin-coated tabloids in one-half grain doses at night. Vedder[8] has treated one case by this method without obtaining the striking results that follow the hypodermic use of emetin, and is therefore not in favor of it.

There is sufficient evidence at the present time to state that emetin should be given by mouth only under circumstances that do not permit of the hypodermic methods or of the administration of the whole drug (ipecac) by mouth, and then only in small doses (one-sixth to one-third grain).

Colonic Route. With reference to this method, Chauffard[9] reports a case of amebic dysentery in which under subcutaneous injections of emetin the stools decreased from fifteen to two or three daily. After reading the report of Marchoux on the treatment of dysentery with emetin enemata, he decided to irrigate his patient with an emetin solution (100 mg. to 1000 c.c.). That day the patient had fifteen dysenteric stools. He looked upon this intestinal intolerance as due to the fact that this patient had been previously treated by subcutaneous injections of the drug.

Although I have never used emetin by enema, I am strongly inclined to agree with Vedder that this so-called intestinal intolerance was due to the direct irritant action of the drug on the intestinal mucosa.

The practical value of solutions of either emetin or ipecac for colonic irrigations is problematical, for the vegetative amebas will be easily destroyed if reached by many of our well-known agents, such as quinin, salicylic acid, silver nitrate, and others, while those in the tissues will not be acted upon.

Dosage and Duration of Treatment. The dosage of emetin origiginally recommended by Rogers was small. The average subcutaneous dose was one-third grain, and a total of two grains usually sufficed for an apparent cure. Later the pendulum swung in the opposite direction and amounts varying from two and one-half to four grains daily were injected subcutaneously, and even by vein in severe cases. The cause of this reaction was probably due to the fact that as time elapsed reports of relapses became more frequent. At the present time the most effective dose appears to be somewhere between these two extremes. For an ordinary case of amebic dysentery in an adult an average of one grain daily is sufficient. It is of course impossible to dogmatize upon this subject, as individualization is necessary. Mild cases may get along well on less than one grain and severe cases may require more. I have yet to see, however, a case that required more than two grains daily, provided the principle of repeated small injections was followed. The tendency in the early days of the emetin treatment was to stop the injections when the stools became formed. Experience has shown that it is better practice to continue the injections, as Dopter advises, for four or five days after the stools are apparently normal. Careful and systematic examination of the stools will be found to be one of the best guides to therapy.

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[7] Administration of Emetin by Mouth in Amebic Dysentery, British Med. Jour., 1913, No. 1, 1369.

[8] Loc. cit.

[9] Resultats inattendus d'un Lavement d'emetine chez un Dysenterique Amebien, etc., Soc. Méd. des Hôp., June 20, 1913.

In general the duration of treatment is from one to two weeks. It is seldom wise to prolong the administration of the drug beyond two weeks even though a diarrheal condition exists unless active entamebas are still present. The diarrheal condition may be due to an intestinal catarrh or an association bacillary infection, or possibly to the drug itself. In two cases that I have recently treated the diarrhea could apparently be attributed to the subcutaneous injections of emetin.

The first case was a college professor of forty years. He was treated by a colleague and put on ascending doses of emetin beginning with one-third grain and increased in four days to two grains a day. During the first few days of the treatment the patient's bowels were checked and the pain and tenesmus subsided. When the large doses of the drug were reached (fourth day) his bowels became loose again and abdominal discomfort returned. When I saw the patient he had taken a total of nine grains of emetin. As no amebas could be found the dose of the drug was reduced for a few days and then discontinued. The patient returned to his home and after two or three weeks the bowel disturbance disappeared. There has been no recurrence in the past four months.

The second case was a young colored male of twenty-eight years who had had a chronic dysentery for five or six years. He was given injections of emetin (one grain) daily for twelve days. Like the former case he at first improved rapidly, then an obstinate diarrhea set in. Examination of the stool showed blood-tinged mucus and a few resting amebas. The emetin was stopped and a saline enema given daily for five days, during which time the number of stools was notably lessened. Following this a short course of emetin by needle was again instituted. At the end of this course the stools were normal and a sigmoidoscopic examination negative.

These two cases favor the view that too large doses of emetin or too prolonged use of moderate doses may cause a diarrhea or be responsible for its persistence. In what way the subcutaneous injection of the drug causes intestinal irritation I am unable to explain. At all events, emetin is best administered in courses of a week to ten days and repeated at intervals if necessary. During the administration of emetin, moderate purgation with castor oil or a saline is often beneficial. It keeps the intestinal tract clean and mechanically washes out many of the entamebas in the gut. For a number of years I have made it a rule not to discharge a patient until he has been given a large dose of salts (one ounce), and the effect on the bowels carefully noted. In some cases that were thought to be cured, dysenteric symptoms returned and active amebas were found in the stools. The salts may be said to act as a therapeutic check upon our cures, though too much reliance should not be placed upon it.

Ill Effects of Emetin. Ill effects from emetin are rarely encountered unless the dosage is large or the administration prolonged for too long a time. I have already mentioned the probability of emetin by needle producing or keeping up a diarrhea. Allen[10] has produced nausea and vomiting by a single dose of four grains; no other ill-effects were noted. A mild peripheral neuritis occurred in a physician under my care who took, while in the country, one and one-third grains of emetin daily for sixteen days. During the last few days of the injections his legs became weak and he suffered with pains especially in the calves. There was also some general muscular weakness. This condition gradually cleared up after stopping the drug. Eshleman[11] reports a case that developed a general eruption, purpuric in character, associated with a severe peripheral neuritis. The patient had received two grains daily for five or six days. Weis[12] has observed peripheral neuritis in two cases following emetin, and believes it to be due to the use of too large doses. Spehl and Colard[13] report a case that had been given one grain for six days and then the dose increased to one and one-half grains daily. After a few days the patient developed a flaccid paresis of all muscles. There was edema of the face, rapid pulse, and diminished tendon reflexes. Recovery was slow. Serious symptoms have been met with after the intravenous[14] use of large doses of emetin. It will be found safer to adhere to the original dose proposed by Rogers for intravenous use (one grain).

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[10] The Emetin Treatment of Amebic Dysentery, Jour. Amer. Med. Assoc., 1913, lx, 664.

[11] Bull. of Touro Infirmary, New Orleans and Surg. Jour., 1914, lxvi, 965.

[12] Ibid.

[13] A Case of Emetin Poisoning, Provence Medical, April 18, 1914, p. 176.

[14] Baermann and Heinemann, Die Behandlung der Amoeben Dysenterie mit Emetine, Münch. med. Woch., 1913, lx, 1132.

In experiments on animals Vedder and Nichols[15] have demonstrated that the drug is fatal to certain laboratory animals in comparatively small doses (2.5 mg. per kg. of emetin intravenously, fatal to rabbit). The evidence is increasing in the literature to the effect that the drug is not as harmless as generally supposed and that large doses are not without danger.

RELAPSES AND CARRIERS. As mentioned in a previous paper[16] it is not always easy to state, in many instances, whether a relapse is a reinfection from within or a fresh infection from without. In reviewing my own cases and the literature in general I should judge approximately 25 per cent. of the cases have recurrences. Under ipecac therapy relapses appeared to be less frequent, though I doubt seriously if this were actually the case. It is quite true that patients once treated with large doses of ipecac[17] rarely return for a second course, at least, to the same physician, for many of them prefer to suffer the inconvenience of the disease or try a patent medicine. On the other hand few individuals object to the emetin treatment and readily return if not cured. Willets[18] believes that the apparent superiority of ipecac in percentages of cures is due to the fact that the dosage of emetin varied widely as well as its mode of administration, while the ipecac cases were treated more persistently than the emetin cases. Siebert,[19] who has had a wide experience with ipecac, considers the effect of emetin more lasting and that fewer cases relapse in the same time with emetin than with ipecac.

The pathology of relapse has already been discussed, and we find that they are due probably to the fact that some of the amebas in the tissues escape destruction by encystment. Attention to the principles of administration, dosage, and duration of treatment previously outlined will prevent relapses in some instances. Where the stools still contain entamebic cysts after apparent cure a recurrence is likely to occur. As these cysts cannot always be found it is a safe rule where possible to place all patients on the intermittent plan of treatment. I have followed, in a general way, Chauffard's[20] method, which consists in giving a second series of injections two weeks after the first, then a third after three weeks, and even a fourth after a like interval. In long-standing cases this may be continued at monthly intervals. The drug is given for four or five successive days. The dosage that I have used has been usually one-third grain, morning and evening. Before instituting the treatment the patient is given one ounce of salts in the morning and the first injection administered after the bowels have acted several times. This method was adopted in the hope that the intestinal congestion and watery stools caused by the saline might produce conditions favorable for the encysted entamebas to again become vegetative, when they would readily be affected by the emetin injections. There is no proof to this effect except, as previously stated, that intestinal irritation favors recurrences.

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[15] Loc. cit.

[16] Lyons, R., Treatment of Amebic Dysentery with Subcutaneous Injections of Emetin Hydrochloride, Jour. Amer. Med. Assoc., 1913, lx, 1216.

[17] Exception should be made in favor of alcresta ipecac which is not disagreeable to take.

[18] Preliminary Report on Treatment of Entamebiasis with Ipecac, Emetin-Neosalvarsan, Philip. Jour. Sci., 1913, ix, 93.

[19] Ueber die Behandlung der Amoeben ruhr mit Emetine, Archiv. f. Schiffs und Tropen-Hygiene, 1914, xviii, 439.

[20] Les Rechutes de la Dysenterie Amibienne et leur Traitment, Jour. des Prat., 1914, xxviii, 38 to 40.

It is too early to predict what the ultimate effect of such plans of treatment will be on the percentages of relapses, as prolonged observation will be necessary. The principle, however, is rational and the number of relapses should be markedly diminished. From our knowledge of the pathology of the disease and the habits of the organisms it was scarcely to be hoped that one course of emetin or any other drug would be curative in every case.

In the treatment of carriers, emetin has not achieved much success. Local irrigations of the bowel are usually resorted to, though emetin is too irritating for this purpose. Fluidextract of ipecac may be substituted. Vedder advises high irrigation with quinin or silver nitrate solution. As it is a question of destroying resistant entamebic cysts, persistent and systematic treatment is required.

EMETIN IN PYORRHEA ALVEOLARIS. The treatment of Rigg's disease with emetin originated from the discovery of Smith and Barrett[21] that amebas were present in the gums of individuals afflicted with the disease. These investigators injected a 0.5 per cent. solution of emetin hydrochloride into the pyorrheal pockets which resulted in marked improvement of the condition. Bass and Johns[22] after an extensive investigation of over 200 cases of Rigg's disease confirmed the observations of Smith and Barrett and concluded that the disease was caused by a specific ameba (*Entamba buccalis*), which could be found in practically every case. They further improved the treatment by the subcutaneous use of the drug, injecting (in any part of the body) usually one-half grain of emetin daily for three to six days. They do not consider local injections of the drug into the gums necessary in every case, but do advise the use of a drop or two of fluidextract of ipecac on the tooth-brush at night. This will prevent further infection or relapses and may also be employed as a prophylactic measure.

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[21] Loc. cit.

[22] Further observations on pyorrhea alveolaris, Bass and Johns, New Orleans Med. and Surg. Jour., Feb., 1915, lxvii, 671.

Four cases were recently reported by the writer[23] in which the disease was apparently cured by the subcutaneous use of emetin. It is too early to consider the question of relapse in this disease or to state whether further injections or courses of emetin will be needed to maintain a cure. The tendency of amebas to encyst and the fact that emetin by needle only affects amebas in the tissues must be borne in mind. In severe cases with pus pockets a combined local and subcutaneous administration of the drug may be required to obtain the best results.

After a few injections of emetin the amebas disappear from the gums and subjective and objective improvement is quickly noted. The tendency of the gums to bleeding, usually so marked in this disease, is rapidly controlled by emetin. This apparent antihemorrhagic effect of the drug in pyorrhea alveolaris is as striking as it is in the dysenteric cases. In both instances it is probably due to the prompt destruction of the amebas in the tissues which, by their activity, are a source of constant irritation and inflammation as well as an important factor in spreading infection. Once these amebas are killed healing occurs very quickly and the bleeding stops. There is no proof[24] thus far that emetin exerts any influence on blood-pressure, coagulability of the blood, or the cell counts.[25] In spite of this the drug has been quite largely employed in the treatment of hemorrhages from many causes and organs. In three cases of hemoptysis the writer[26] was unable to observe that the drug possessed any antihemorrhagic qualities, and believes, therefore, that most of the favorable reports are due to the well-known tendency of hemorrhages to spontaneous arrest.

Very recently in five out of seventeen excised tonsils amebas have been demonstrated by Smith, Middleton, and Barrett. The exact role played by the amebas in such cases is not definitely determined. In any event they are a complicating factor and tend by their activity to keep up chronic irritation and prevent healing. The above-mentioned observers lay stress upon the fact that the amebas feed largely upon the accompanying bacteria, and in their bacterial phagocytic action they doubtless set free different endotoxins. The end results of this toxic absorption will therefore vary in their manifestations according to the kind of microörganisms ingested. In one of the nine clinical cases reported by the authors the patient suffered from a multiple arthritis. Amebas were found in the tonsils and also in the gums. Emetin in small doses apparently relieved the arthritic symptoms after the salicylates had failed.

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[23] Lyons, R., Emetin Hydrochloride in the Treatment of Amebiasis and Other Affections, read before Southern Medical Association, November 11, 1914.

[24] Flandin, Emetin in Hemoptysis, Soc. Med. des Hôp., July 18, 1913.

[25] Maurel (Bull. de l'Acad. de méd., March 24, 1914, cited from Prog. Med., December, 1914, p. 348) claims that emetin acts electively on smooth fibers and particularly on those of the bloodvessels, causing them to contract. This vasoconstriction explains, in his opinion, the influence of emetin on hemorrhage. On the other hand, Maurel states (Arch. de méd. et d'Anat. Path., May, 1914, xxvi, 3, p. 225) that the apparent beneficial action of emetin in arresting hemorrhage is all the more to be wondered at, seeing that experimentally in animals it has proved to have no action as a vasoconstrictor.

[26] Loc. cit.

That amebas may be found complicating or causing other pathological conditions is not improbable, but until this is shown to be the case the heterogenious use of the drug in all sorts of affections is hardly to be recommended, as it will tend to throw discredit upon one of the most valuable therapeutic agents we have at our command.

Summary. The chief points brought out may be briefly summarized as follows:

1. Ipecac and emetin when taken by needle or by mouth act through absorption into the blood stream and exert their specific effect only on those entamebas within reach of the circulation, that is, in the tissues. Entamebas free in the lumen of the gut are apparently not affected by either the oral or subcutaneous use of emetin or ipecac.

2. It is not definitely known how or in what form ipecac and emetin are eliminated from the body, but there is some experimental evidence that the amebicidal principles of ipecac (emetin) when taken by mouth are not eliminated in the feces.

3. The failure of the emetin by needle to destroy the vegetative *Entameba coli*, a parasite simply harbored in the intestinal canal, argues against the elimination of the drug from the circulation by way of the large intestines.

4. Relapses are due to the survival of some of the entamebas probably through encystment. There is reason to believe that in the majority of relapses some of these cysts remain embedded in the tissues of the gut, only awaiting favorable conditions to become vegetative.

5. In the carrier state the entamebas are probably simply harbored in the lumen of the gut in the same manner as the coli, thereby causing no symptoms. The intestinal mucosa is in some way protected against the penetration of the organism.

6. Emetin is best administered subcutaneously. Small, repeated injections are to be preferred, as they are more rapidly absorbed and the effect is maintained. In severe cases emetin should be used intravenously.

7. The oral administration of emetin is not advisable because of the intestinal irritation that results. The whole drug is preferable for this route. For the same reason emetin is not suited for colonic irrigations.

8. In an ordinary case of amebic dysentery an average of one grain daily or less is sufficient. The duration of the treatment is from one to two weeks. Too large doses or too prolonged use of

moderate doses may cause a diarrhea or be responsible for its persistence. There is increasing evidence that large doses of emetin are not without ill effect.

9. In order to prevent relapses an intermittent form of treatment should be instituted in every case even though cysts are not found.

10. Emetin, subcutaneously and locally, has been shown to be practically specific in pyorrhea alveolaris.

11. The use of emetin in hemorrhagic conditions is entirely empirical and its value is questionable.

TREATMENT OF SCOLIOSIS.

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There are two principal forms of lateral curvature of the spine which present themselves to the practitioner's attention, (1) the functional or the static form, and (2) the rotary or the organic variety. So much attention has been given of late to the treatment of the rotary form that the consideration of the functional type has been largely neglected. Since many of the rotary cases have at some period been of the functional type, and have taken on the rotary form through neglect or inefficient treatment, the consideration of the functional form becomes a matter of paramount importance. In order to determine the presence of the primary form it is necessary to recognize the functional type of the affection and to distinguish it from the rotary or organic type. This can be determined by:

1. The history of the case. There are certain etiological factors which should always first be considered before undertaking the treatment of any case of scoliosis. The history should include the birth, whether natural or instrumental; if employed, the occupation; the age at the onset of the affection; any visual errors; the effect of puberty or of any antecedent illness which might have led to general debility, such as fevers, pulmonary affections, acute exanthemata of youth; the diet from birth, especially such as would tend to produce rickets; inherited tendencies, especially tuberculosis; the inheritance or acquisition of nervous affections, such as dystrophies, infantile paralysis, unilateral development; congenital defects of the spine; or the loss of a member from congenital absence, disease, injury; or finally the inequality of the

lower extremities from any of the many causes which produce this deformity.

2. The examination of the patient in Adams' position.

3. The recognition of the functional form from the lateral blending of the English.

Of the functional type several groups are classified according to their etiology, and these include the habitual, the true static, and the occupational.

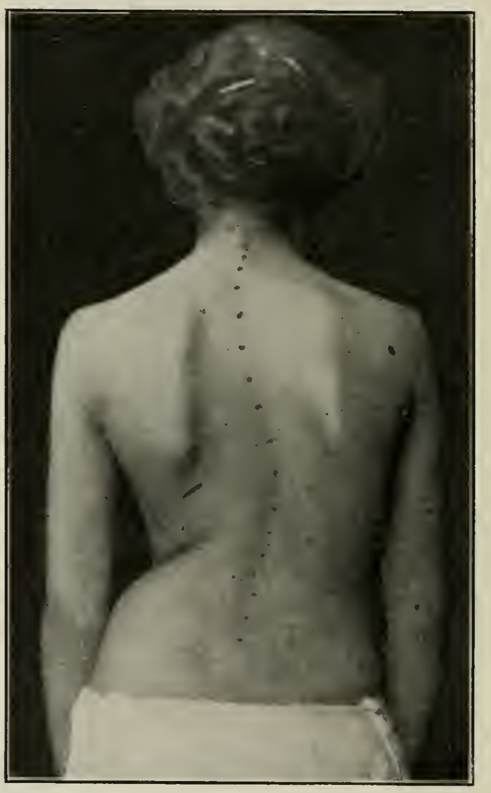

Fig. 1.—Right dorsal scoliosis.

The *habitual* results from partial or unequal use of the muscular system, the faulty positions being assumed either from carelessness or fatigue, as a single instance may be mentioned the scoliosis to be observed in artists' models that have become deformed from assuming certain positions for long periods of time.

In the *static* form there is an inequality resulting from alterations of one extremity. Whatever produces a shortening of one lower extremity produces an obliquity of the pelvis in the opposite direction, and a primary deviation of the lumbar vertebræ. This may result from destructive changes in the articular structures, flat-foot, back-knee from ligamentous relaxation, etc.

As indicated by its appelation, *occupational* scoliosis results from oblique positions assumed during occupations. Lateral curvature in youth is specially liable to affect those whose work requires them to bear heavy burdens upon one side. The habitual is most amenable to treatment.

In order to recognize more accurately the functional form the organic must at once be clearly differentiated. These are the true rotary forms, and their diagnoses rest upon the following factors:

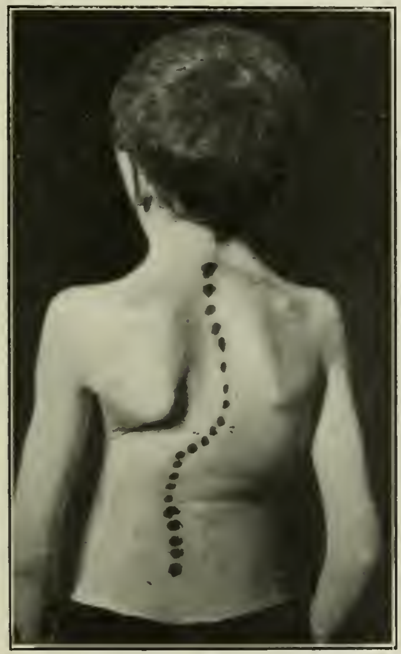

FIG. 2.—Severe double curve due to rickets.

(1) The Roentgen-ray examinations. (2) Examination in Adams' position, in which attitude the curve persists as a permanent deformity on the convex side. (3) By suspension, in which position the curve is only slightly affected.

Of the organic group some of the types of cases are amenable to correction by forcible methods of treatment. These are the cases of the functional type that have gradually become more severe, and to which rotation and torsion have been added, and in which the structures have become firm and unyielding, giving the so-called "fixed curves." The organic forms not amenable to treatment are those due to infantile paralysis, to suprenumerary bones and enlarged processes, empyema, bone-softening, and rickets.

TREATMENT OF THE FUNCTIONAL FORM. For many years this variety of scoliosis has been treated by orthopedic surgeons, with much success, by exercises and corrective measures. Many years ago the writer presented a method of treating these forms by a series of gymnastic exercises.[1] This method of treatment, thus advocated, has been used to the present time, and is still employed with much satisfaction in this type of cases, and to it has been added certain manipulations and mild forcible corrective measures which make it extremely valuable in the treatment of these secondary forms of scoliosis. The best results are obtained in private practice but where individual work can be substituted for class work the results in hospital cases are very gratifying. Systematically arranged these measures are as follows: (1) Development of weak muscles by exercises adapted to them individually or collectively; (2) slight over-development of the weak muscles; (3) uniform development of all the muscles; (4) employment of special movements to prevent relapse.

To successfully treat this class of cases it becomes incumbent upon the surgeon to discover the best voluntary position that can be assumed by the patient to correct the deformity and then in taking all the exercises in that position or in favoring that position in the use of all movements. Such a procedure of necessity leads to the development of the muscular structures, on the concave side of the deformity, and of the stretched or atrophied muscles on the convex aspect, these exercises to be continued or modified until slight overcorrection has been secured. Each case is a study in itself, and while individual sets of exercises are prescribed for certain curves, experience has amply demonstrated that certain combinations of exercises are best adapted and are capable of yielding the best possible results, in very many cases, that offer themselves for treatment. These exercises must be taken under the supervision of the surgeon, the trained instructor, or the masseuse. They are to be indulged in once a day, from thirty to forty minutes each; and two hours after or one hour before a meal. Massage is to follow, and afterward the patient must lie in the prone position or the keynote position, for a half-hour to an hour. The keynote position for right dorsal scoliosis (the more usual variety) is with the right arm extended sideways and the left arm elevated by the side of the head. These exercises are to be continued daily for six weeks, or tri-weekly for three months, and at two periods of the year, except during the menstrual periods and on Sundays. They are given three or four at a time by the surgeon until the whole series has been mastered, and should never be carried to the point of fatigue. Throughout the exercises normal breathing should be indulged in, and at the end of each exercise one or two full breaths should be taken. If other work conflicts with the course of treatment it is necessary to omit all duties, school-work, etc., so that the patient may conscientiously comply with the requirements as laid down by the surgeon.

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[1] International Clinics, 1898, vol. ii, eighth series.

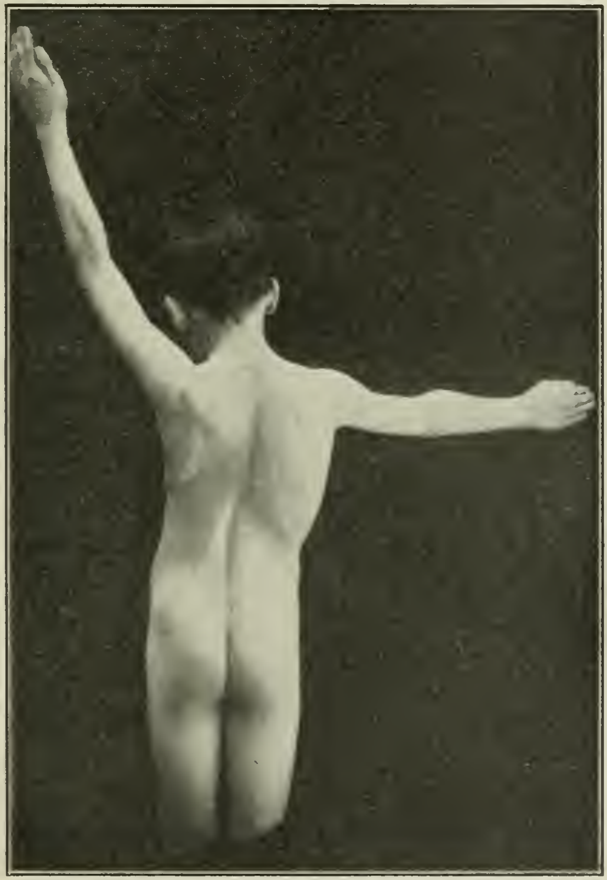

FIG. 3.—Right dorsal curvature. Key-note position.

The medical treatment should be directed by the family physician. He may build up the patient by the employment of tonics and remedial agents such as come within his province. Menstrual irregularities will be corrected as soon as the scoliosis is corrected. Flat-foot or any asymmetry in the lower limbs should engage the serious attention of the orthopedic surgeon as well as any injury to the hip or knee. Visual errors should be corrected by the ophthalmologist.

The special exercises in right dorsal scoliosis, which is the more common form (the treatment for left dorsal scoliosis being just the reverse), are as follows: (1) Best standing position: head up; abdomen in; chest *up* and *forward;* weight on balls of feet; (2) keynote position, which is, left arm upward, stretch; right arm sideways, stretch; (3) same as (2) with "trunk forward, bend;" (4) same as (2) with "trunk to right, bend;" (5) same as (2) with "trunk diagonally forward, bend;" (6) same as (2) with "heels raise;" (7) same as (6) with "knees bend;" (8) same as (2) with "right foot outward, fall out."

Additional exercises should be given to correct the irregularities in the lower extremities and to obliterate the secondary lumbar curve.

After the curves have been overcorrected, bilateral exercises must be used for the symmetrical development of the body. These may selected from the Swedish exercises or combined, so as to bring into play all the muscles of the body, by employing the following eight exercises, arranged by Dr. Keating and myself: (1) "Neck firm;" then "heels, raise;"[2] (2) "neck firm, trunk to left and right twist;" (3) "arms upward, stretch;" then "trunk to the left and right, bend;" (4) "arms upward, stretch; "then "trunk forward, bend;" (5) "right (or left arm) upward stretch;" then "right (or left) foot outward, fall out;" (6) "arms upward, stretch;" then "right (or left foot) outward, fall out;" then "trunk twists toward the side, corresponding to the forward foot;" (7) "arms sideways, raise;" "right (or left) foot forward, fall out;" (8) "arms upward, stretch;" "heels raise;" "knees bend."

APPARATUS. In the treatment of these cases, certain apparatus will be found valuable, especially the high plinth of the Swedes, stall bars, and certain stretching apparatuses and appliances, such as the lateral suspension apparatus of Redard, Beely and Lorenz, which will be found invaluable. Suspension may be facilitated by the use of rings, various kinds of ladders, trapeze, etc.

BRACES. In the treatment of mild cases of functional scoliosis, braces are seldom necessary, but a light corset-support, of the Shaffer type, as modified by the writer, is useful as a reminder to the patient, to assume a correct position, and offering a slight support to the patient during the intervals of exercise and recumbency. It should be made of light steel or duralamin,[3] and may be incorporated into a corset or worn under the corset. It consists essentially of a waist band, steadied by vertical pelvic bands, from which is built up a crutch, beneath the depressed shoulder, and a pressure-pad over the deformity.

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[2] Cyclopedia of the Diseases of Children, Keating, year, vol. iv, p. 318.

[3] Duralamin is the new orthopedic metal, employed in the arts, made by the manufacturers of the celebrated Maxim guns. It is employed in the construction of air ships and submarines, and was introduced by the writer to the notice of the Medical profession (Orthopedic Transactions, September, 1913). It is almost as strong as steel, and but one-third as heavy, and is more stable than aluminum.

HISTOPATHOLOGY OF CALCIFICATION OF THE SPINATUS TENDONS AS ASSOCIATED WITH SUBACROMIAL BURSITIS.

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Under the title "Prevalent Fallacies Concerning Subacromial Bursitis; its Pathogenesis and Rational Operative Treatment," Brickner has described[1] his observations, surgical and radiographic, of calcareous deposits in and upon the supra- and infraspinatus tendons, associated with adhesive subacromial bursitis. The following is based upon the histological study of portions of diseased tendons in four of his cases.

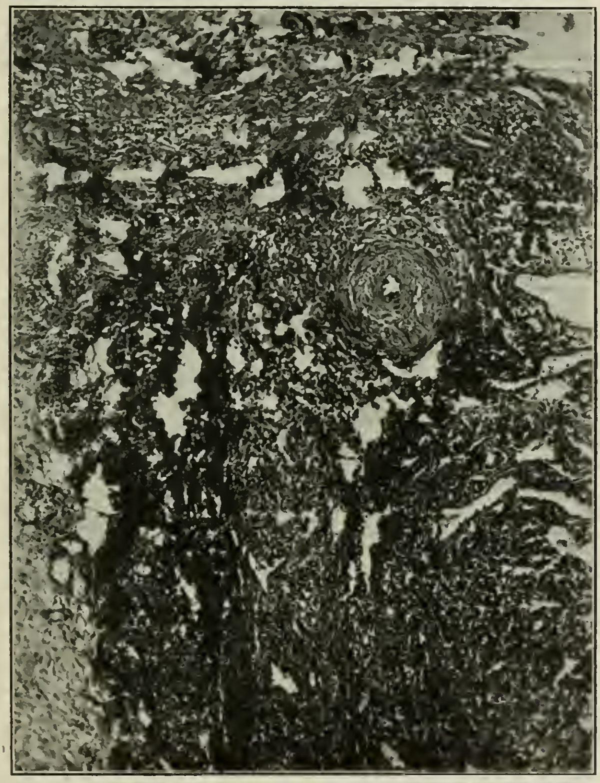

Fig. 1.—Case 1. Showing intratendinous formation of young granulation tissue and formation of new bloodvessels. To the left, a narrow zone of older organized connective tissue.

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[1] Amer. Jour. Med. Sci., March 1915, cxlix, 351.

CASE I.—Female, aged forty-five years. Operation upon the sixteenth day after indirect trauma. Fresh adhesions in and ecchymosis of bursa; yellow, semiliquid calcareous deposit overlying and within laceration of swollen supraspinatus tendon; infraspinatus infiltrated with blood.

Pathological Examination (Figs. 1 and 2). Section shows a crescentic mass of tissue. Covering the entire convex border is a narrow zone of fairly loose connective-tissue fibers—a comparatively sparse number of large, long spindle-shaped cells of the connective-tissue type, a fair sprinkling of round cells, a few red blood cells, a few thin-walled bloodvessels. This tissue represents a fairly well-organized granulation tissue.

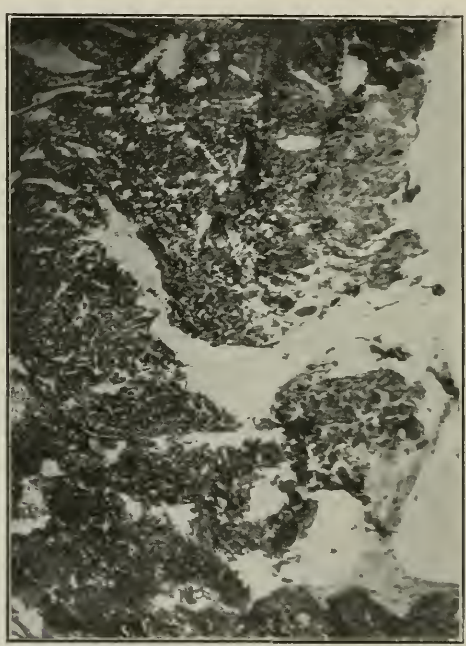

FIG. 2.—Case 1. Necrotic tendon lying within granulation tissue containing small discrete deposits of lime.

Within this zone and filling the cavity of the crescent is a mass of tissue appreciably more cellular. The general appearance is that of an early form of granulation tissue. The predominant cell type is the round or plasma cell. There are a small number of spindle shaped connective-tissue cells and a few old and many newly formed bloodvessels. This tissue is abundantly infiltrated with red blood cells, most of which show degeneration changes, showing that the hemorrhage antedates the operation. The few old bloodvessels are small in size, and have thickened walls; this thickening is largely due to swelling of the intima. The newly formed blood-vessels are irregular in shape and size, and consist mainly of clefts or spaces within the granulation tissue lined by a distinct and uniform row of endothelium.

Upon the innermost aspect of this area of young granulation tissue there are finely granular amorphous masses of necrotic tissue. While this necrotic tissue stains diffusely with eosin, here and there are scattered discrete sand-like particles, that stain blue with hematoxylon, indicating a lime reaction. The greater part of this necrotic tissue lies loosely within the cavity of the crescent; a much smaller portion is still in direct continuity with the adjacent granulation tissue.

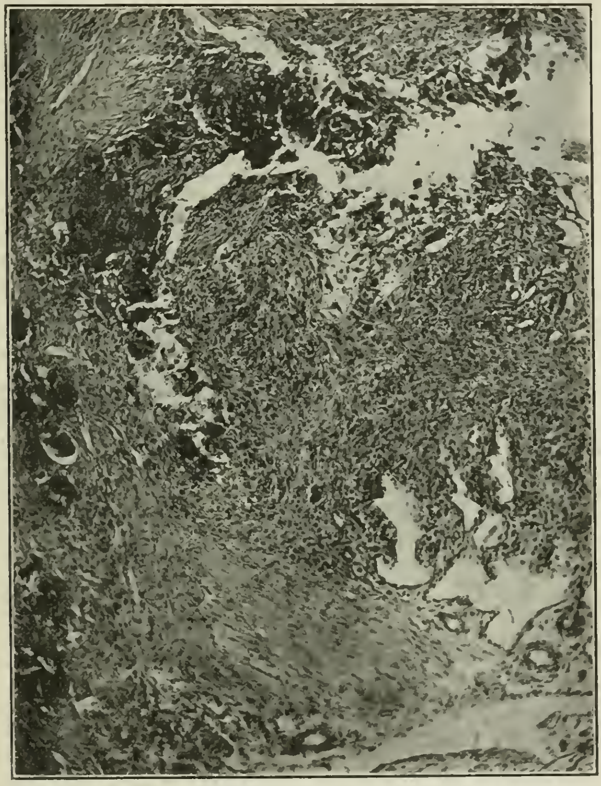

FIG. 3.—Case 2. Well-organized granulation tissue springing from a tendon that has undergone extensive hyaline degeneration. Small discrete lime deposits lying within the tendon and in the granulation tissue. Here and there a foreign body giant cell.

Epicrisis. This section reveals substantially two stages of granulation tissue: an outer, the older, which may be interpreted as representing the wall of a focus of inflammation; and an inner, a more recent variety. In addition, there is within the centre of this focus necrotic tissue. This has undergone partial calcification.

Diagnosis. Necrosis of tendon with partial calcification and young granulation tissue.

Case II.—Indirect trauma four or five months previously. Male, aged thirty years. Extensive adhesions in bursa; finger-nail-sized, gritty, yellow deposit entirely within supraspinatus tendon about 5 cm. from its insertion.

Pathological Examination. Sections show two different masses (Figs. 3 and 4). The first and larger consists of an irregular mass of tendon tissue continuous with a large area of granulation tissue. The tendon consists of firm fibrous longitudinal bands of connective-tissue, portions of which show hyaline degeneration. Only a small area of tendon fiber is present; the rest have undergone extensive calcification. The calcification is present either in the form of discrete, sharply circumscribed, sand-like masses embedded, as it were, in a cavity within the tendon; or as diffuse finely granular masses, shading imperceptibly into the surrounding tissue structure; or as finely granular amorphous material lying within the tendon or the granulation tissue.

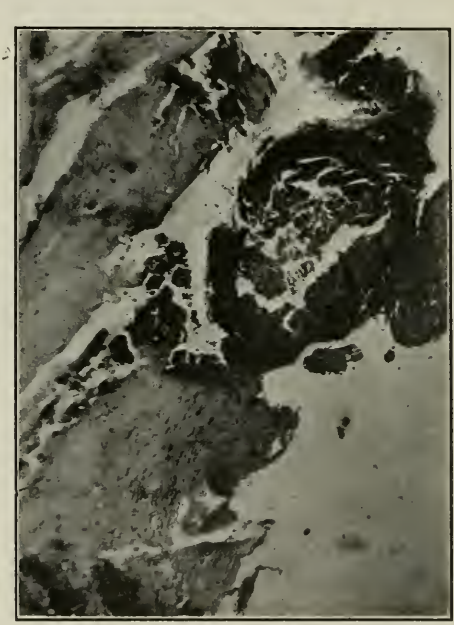

Fig. 4.—Case 2. Tendon tissue that has undergone extensive hyaline degeneration and calcification.

The granulation tissue is richly cellular, almost sarcomatous in appearance, and consists of large oval or spindle-shaped cells with a finely fibrillar intercellular connective-tissue. There are many delicately walled newly formed bloodvessels. A few giant cells are present, some in relation to the lime granules, some not. They are all probably so-called "foreign body" giant cells.

The second and smaller mass consists of hyaline tendinous tissue which has undergone almost complete calcification. The lime deposit consists of finely granular masses, either within the tendon or upon its surface.

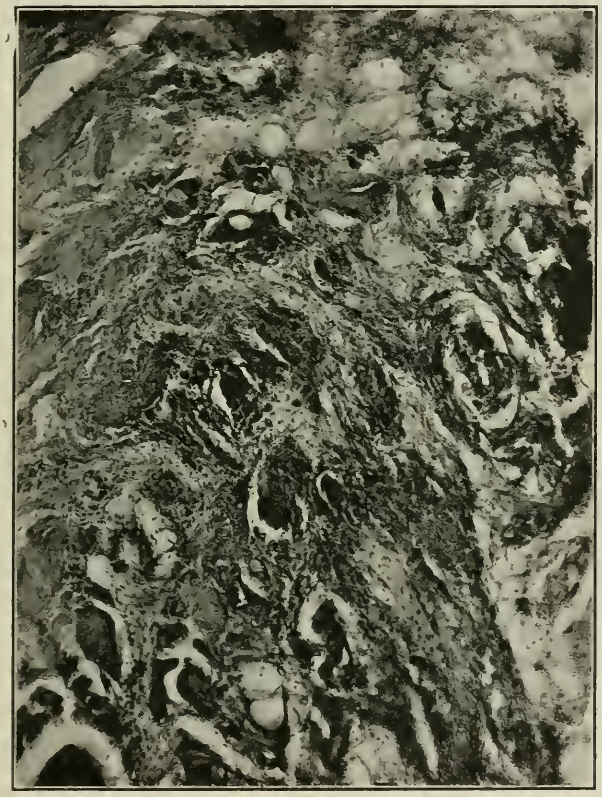

Fig. 5.—Case 3. Tendon bundles separated from one another by extensive scar tissue.

Epicrisis. A tendon that has undergone extensive hyaline degeneration and calcification. There is manifest necrosis with secondary calcification of the tendon. In addition, there is a comparatively early form of granulation tissue.

Diagnosis. Chronic tendinitis, with necrosis, hyaline degeneration, and calcification, and the formation of granulation tissue.

Case III.—Chronic (one and a half years). Female, aged about forty-five years. No history of trauma. Persistent "brachial neuritis." A few fine adhesions in bursa; small, dry, gritty, yellow-white lime deposit, entirely within infraspinatus tendon near its insertion.

Pathological Examination. With the low objective the section shows essentially a mass of tendon tissue encircling a cavity which contains necrotic detritus (Figs. 5 and 6). The tendon tissue consists of dense strands of fibrous tissue which is grouped in longitudinal strands or bundles. Between many of these bundles is loose cellular tissue, consisting of coarse fibrous tissue, many spindle-shaped connective-tissue cells, and a small number of delicate-walled bloodvessels. In some areas the tendon bundles have undergone hyaline degeneration. The cavity within the tendon contains a finely granular amorphous mass of necrosed material which in part lies loosely within the cavity and in part is continuous with the fibrous wall of the cavity. No calcification is present, although Dr. Brickner assures me that much gritty material was found at operation. The lime must have been shaken out of the specimen during manipulation.

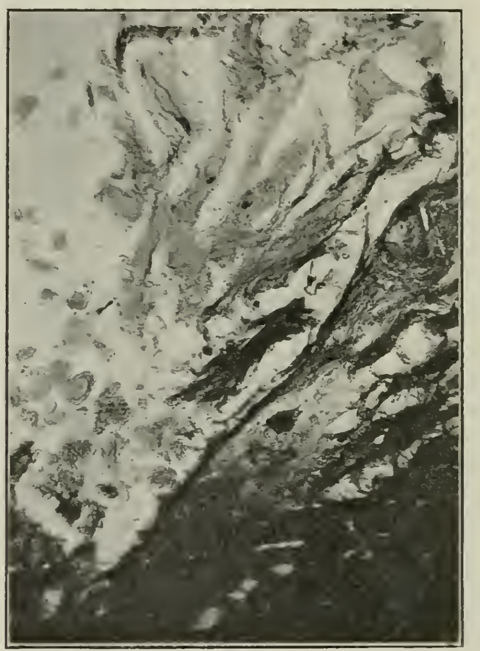

FIG. 6.—Case 3. Wall of cavity within tendon containing necrotic tendon tissue.

Epicrisis. This section represents a tendon between the bundles of which firmly organized tissue has formed. The tendon bundles have in part undergone hyaline degeneration. Within the tendon is a cavity containing necrosed material.

Diagnosis. Chronic tendinitis with hyaline degeneration.

Case IV.—Acute. Male, aged about sixty years. Operation seventeen days after direct injury. Well-developed adhesions in bursa; two discrete white powdery deposits in supraspinatus tendon.

Pathological Examination. Sections reveal a thin rind of tendon tissue enclosing a cavity containing finely granular necrosed material. Within the tendon tissue are extensive areas of necrosis, most of which take the lime reactions with hematoxylon. The necrotic material within the cavity also shows extensive areas of calcification. In no specimen was the slightest reactive tissue noted, in the form of round-celled infiltration, granulation tissue, or the formation of new bloodvessels.

Diagnosis. Necrosis and calcification of tendon.

Summary. The first three cases exemplify three stages of a lesion that may be termed "tendinitis." The common factor is the formation within and around the tendon fibers of granulation tissue which corresponds in a general way, according to morphological criteria, with the duration of the illness. We find, accordingly, a progressive organization of the reactive inflammatory tissue in and around the necrosed portions of the tendon, so that a mere round-celled infiltration with early formation of bloodvessels in the first case becomes a scar-like tissue, with fully developed bloodvessels in the third. The last case shows no reactive tissue around the dead portions of the tendon, although the duration of illness was practically the same as in the first case. The only way we can account for this absence is the age of the patient, at which time the reaction forces of the body are notoriously deficient.

Necrosis. Another common factor in all four cases is the presence of necrotic tissue. It has the same morphological appearance in all, namely, a finely granular, amorphous, and completely acellular mass. In Cases I, II, and IV this necrotic tissue is more or less calcified. Topographically the necrotic tissue has two relations: either in direct continuity with the tendon, or with a greater or smaller zone of granulation tissue intervening.

The necrotic tissue can have only two sources: (1) the degeneration of the blood and serum consequent upon the primary trauma; (2) the breaking down by coagulation necrosis of the tendinous structures. The first origin can obviously be excluded for the following reasons: (*a*) There is no blood pigment; (*b*) the appearance of the tissue is too homogeneous and plastic to arise from a fluid origin; (*c*) the continuity between the necrosed area and the surrounding solid tissue is a gradual one, so that it is impossible to determine a sharp definition between the well-preserved and the necrotic areas. Were the necrosis of fluid origin we should expect a cyst-like cavity. I conclude, therefore, that the necrosis arises from actual death of tendon. The explanation of the necrosis is obvious. The blood supply of a tendon is notoriously meager. The tendon bundles proper have no blood supply. Whatever bloodvessels the tendon contains are present only in the connective-tissue left between the tendon bundles (Stöhr), and these are small in size and number. It is, therefore, readily understandable how a trauma, however slight, may interfere profoundly with the blood supply of a given area of tendon and thereby cause necrosis.

Calcification. Lime is found in Cases I, II, and IV. In Case III Dr. Brickner assures me that he found gritty masses at the operation. The failure to find lime microscopically, therefore, may be regarded as accidental, due, in all probability, to the fact that the lime deposit was shaken out in the subsequent manipulation of the specimen.

The lime is present in three forms: (1) as small sand-like particles within the necrosed tissue; (2) as diffuse massive calcification of the necrosed tissue; (3) as isolated discrete and sharply defined nodules embedded within the tendon or the granulation tissue. Furthermore, Brickner reports calcification in some cases upon the surface of the tendon, in the form of a thick, white, gritty material, associated with a minute tear of the tendon. He has also found at operation, and by Roentgen-ray, multiple deposits in the tendon, sometimes at a considerable distance from its insertion. In some cases the shadow-forming deposit is quite liquid, and this occurs in early as well as old cases, in extra- as well as intratendinous deposits.

What is the pathogenesis of this calcification? At the outset it is necessary to settle the question whether these tendinous calcifications are due to injury of the humerus, by the statement that neither Brickner nor any other observer has ever seen any direct connection of the deposit with the bone, either by Roentgen rays or at operation.

The pathogenesis of calcification within tendons is governed by the same conditions that apply to abnormal calcifications in other parts of the body. It has been definitely established that calcification only occurs in dead or inert tissue, that is, tissues that have no blood supply. It never occurs in tissues whose blood supply is abundant. Familiar examples of calcification in necrosed tissues are those in caseous tubercles, atheromatous plaques, old abscesses, infarcts, and old sebaceous and dermoid cysts. Furthermore, calcification has a peculiar predilection for connective-tissues that have undergone hyaline degeneration, which also is merely a form of necrosis. This is commonly noted in fibromyomata of the uterus of long standing. I have also noted this phenomenon in the hyaline corpora albicantia of the ovary; in the wall of a chronically inflamed tube; in old pleuritic thickenings; in the walls of hydatid cysts; in old scars, etc. Furthermore, it is an interesting observation that wherever we find a deposit of lime, we are apt, at the same time, to find partial ossification of the tissues. The conditions under which ossifications form after calcification are not precisely understood, but they probably depend upon two factors: (1) a sufficient period of time and (2) the formation of a reactive blood supply. We predict, therefore, that an extensive study of calcified tendons will sooner or later discover an instance of ossification. This point will again be discussed in greater detail.

Causation of Early Calcification. Brickner[2] calls attention to the remarkably early appearance of the calcification in these cases. In addition to the first and fourth cases, in which the lime deposit was demonstrated, roentgenographically, upon the tenth and eleventh days respectively following the injury, Brickner has found the deposit by roentgenography as early as twenty-four hours and five days after trauma.

Now, in all the instances of pathological calcification that we have considered it has been generally accepted that the deposition of lime occurs only when the necrosis is of long standing. Calcification of a tissue, in other words, is generally regarded as indicating chronicity of the lesion. How, therefore, are we to account for the very early calcification noted in these cases?

It seems to me that sufficient explanation of this phenomenon is found in the observations upon experimental calcification. Litten[3] and Lick[4] found lime microscopically in necrosed portions of the kidney, one day after ligature of the renal artery. Especially significant for our purposes are the observations of Schujeninoff,[5] who found calcification of the muscle fibers both in man and in animals one and a half days after the suture of a divided muscle. The lime in every instance was near the suture line, and the affected muscle fiber was the seat of colloid degeneration. Schujeninoff believed that the calcification was due to interference with the circulation by the ligation of small bloodvessels. I have frequently seen calcification of necrosed portions of malignant growths when the duration of necrosis could be reasonably reckoned in terms of days.

Strangely enough, the repeated observations upon experimental healing of tendons fail to throw any light upon the problem of the early incidence of calcification in the spinatus tendons. Studies upon the injury and repair of tendons are numerous enough, the more comprehensive being those of Palla,[6] Seggel,[7] and Yamagiva.[8] I have studied the extensive protocols of these writers carefully, and in not a single instance was calcification of the tendon noted. The absence of calcification is puzzling, and can be accounted for only by the fact that the tendo Achilles, exclusively employed for experimental purposes, presents some peculiar biological properties that do not predispose it to calcification. In order to satisfy ourselves upon this point, we propose, at some future date, to repeat these experiments upon the spinatus tendons.

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[2] Loc. cit.

[3] Ztschr. f. klin. Med., 1880, v. i.

[4] Arch. f. klin. Chir., 1908, lxxxv, 118.

[5] Ztschr. f. Heilk., 1897, xviii, 79.

[6] Beitr. z. klin. Chir., 1909, lxiii, 644.

[7] Ibid., Chir., 1903, xxxviii, 342.

[8] Arch. f. Path. Anat., Virchow, cxxxv, 308.

At all events, there is already ample evidence in certain tissues, at least, that calcification in necrotic tissue occurs earlier than is generally believed. In all probability the early or late incidence of calcification depends upon peculiar predilections of certain tissues, due to chemical affinities the nature of which has not been precisely determined (Adami).[9] This will explain why calcification occurs oftener in some tissues than in others. Wells[10] accounts for the greater frequency (in his experience) of calcification in the lungs, stomach, and kidneys by the fact that these organs have an acid secretion which precipitates carbonate of lime. This contention is hardly tenable in view of the fact that some of the commonest lime deposits arise in tissues that are constantly bathed in alkaline juices, for example, arteriosclerosis. To explain the early calcification in tendons, we suggest that perhaps it is the collagen, present in the tendons, according to Gies and Buerger,[11] to the extent of 37 per cent., that acts as the lime precipitant. This suggestion arose from the observations of Schujeninoff,[12] who showed that the muscle fibers in which lime deposition occurred were in a state of colloid degeneration—a condition chemically allied to collagen; and, furthermore, by the affinity of cartilage (which is also rich in collagen, (Hammersten[13]) for calcification.

Maturity of the patient is unquestionably a large factor in determining calcification of tendon, and, indeed, of other tissues as well. Calcification is extremely rare in children and youth, and becomes progressively more frequent as age advances. This explains why subacromial bursitis with calcification of the spinatus tendons has never been observed in the young.

Previous Pathological Studies upon Calcification of the Spinatus Tendon. As far as we are aware, no previous systematic study has been made of the pathogenesis of the lesion underlying the symptom-complex embraced under the term "subacromial bursitis." There are only two pathological reports upon excised portions of tendons, that of Wright, in one of Codman's[14] cases and that of Wrede.[15]

Wright's report was "microscopic examination of the material from your case of 'sub-deltoid bursitis' shows the following: The main constituent of the material is a coarse, dense, fibrous tissue. Associated with this is a looser connective-tissue in which are enclosed bloodvessels and a good many cells of the lymphocyte series. The coarse, fibrous tissue in some places contains more fibroblasts than elsewhere, and may therefore be considered to be in process of growth at these points. In a few places it is necrotic, and it contains few bloodvessels. I can not find any evidence of tuberculosis. The material seems to me to show a slow, productive inflammatory process combined with degeneration and necrosis similar to the process observed in the heart valves in some cases of chronic endocarditis."

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[9] Principles of Pathology, Philadelphia, 1914.

[10] Arch. Int. Med., vii, 721.

[11] Amer. Jour. Physiol., December, 1901.

[12] Loc. cit.

[13] Text-book of Physiological Chemistry, Trans. from 7th German ed., 1911.

[14] Boston Med. and Surg. Jour., 1908, clix, beginning October 22.

[15] Arch. f. klin. Chir., 1912, xcix, 259.

Wrede's case: Man, aged seventy-six years, who had suffered for one year following a trauma. At operation a deposit within the supraspinatus tendon was found. From this portion a small piece was excised. The tendon was found necrotic with deposition of lime. In addition there were granulation tissue and giant cells. These findings, therefore, correspond to our own. Wrede enters into a prolix discussion of the etiology of the malady, and finally assumes a non-committal attitude.

Analogy of the Lesion to Other Pathological States of Tendons. Calcification of the spinatus tendons, following so soon after trauma (the etiology described by the more extensive observers of this malady, Brickner and Codman), has, as far as I am aware, no precise analogy in human pathology. This singularity is especially striking when we consider that the trauma in most of the cases is slight or trivial, merely sufficient, as Brickner and Codman declare, to jam the spinatus tendons between the head of the humerus and the acromion process. The thought obviously suggests itself, Why are other tendons, such as the tendo Achilles and those around the knee and elbow which are more frequently subjected to trauma, free from such calcification? The answer is that such calcifications probably do occur, although the pathological proof is thus far lacking.

Since the introduction of the Roentgen rays, shadows in tendons, especially in the neighborhood of joints, are a frequent finding. As instances, we cite the not uncommon calcification or ossification in the tendo Achilles arising in continuity from the posterior aspect of the os calcis (Höring,[16] Jacobsthal,[17] Haglund,[18]), but sometimes isolated within the tendon (Blencke,[19] Finney,[20]); also to the frequent ossification of tendons around joints following sprain or fracture, for example, the triceps (Engelbrechtson,[21] Fragenheim[22]), brachialis anticus (Tyson[23]), adductor longus (Boyd,[24] Whitelock[25]), obliquus externus (Charles[26]), quadriceps femoris (Bähr[27]), gastrocnemius and deltoideus (Whitelock[28]). The cases of so-called "riders' bone," *i. e.*, formation of bone within the tendons of the adductors of the thigh, and "drill bone," in the insertion of the deltoid, probably also belong to this group of traumatic "ossifications" of tendons. These citations prove that traumatic "ossifications" do occur, although by no means commonly. I have purposely cast doubt upon the validity of the osseous formation by the use of quotation marks for the reason that, with the exception of the case of ossification of the tendo Achilles, reported by Jacobsthal, the pathological proof of the presence of bone is entirely lacking. It is by no means proved that some of the shadows reported as bone by various observers may not have been those of lime concretions.

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[16] Deutsch. med. Wchnschr., 1908, xxxiv, 175.

[17] Arch. f. klin. Chir., lxxxviii, 146.

[18] Ztschr. f. orthop. Chir., xix, 457.

[19] Ibid, 1908, xx, 363.

[20] Quoted by Binnie, Keen's Surgery, vol. ii.

[21] Railway Surg. Jour., 1911–1912, xviii, 320.

[22] Med. Klinik, 1909, v, 278.

[23] British Med. Jour., April 16, 1910.

[24] Clin. Jour., London, 1897, x, 186.

[25] Sprains and Allied Injuries of Joints, London, 1909.

[26] British Med. Jour., 1912, i, 949.

[27] Quoted by Engelbrechtson.

Whether these shadows are of lime or bone is, for our purposes, a matter of indifference, for the reason that, as most pathologists have agreed, calcification always precedes abnormal ossification. These shadows at some stage of the process must have been those of pure lime deposits. The earlier stages of bone formation are precisely those that we have described in our tendon specimens, namely, death of tissue with calcification. I have never, nor, as far as I am aware, has anybody else, seen an area of ossification occurring *de novo* in normal tissue.[29]

This postulate leads us to predict, as I have said before, that when more of these calcified spinatus tendons are examined, bone will sooner or later be found.

The demonstration, therefore, that calcification always precedes ossification removes whatever doubt may have arisen as to the validity of the analogy between the traumatic calcification of the supraspinatus tendon and the supposed bony lesions that we have enumerated.

The mere demonstration of an analogous traumatic lesion of the tendons by no means accounts, however, either for the peculiarly common or for the early incidence of calcification of the spinatus tendons. The lesions in the other tendons to which I have referred are infrequent, and the manner of the process indicates that the calcification must have come rather late upon the trauma. The lesions in the spinatus tendons, on the other hand, are comparatively common, as proved by the experience of Brickner, who has seen over twenty cases within the last two years. The early and common incidence appearance of lime in these cases has no precise counterpart, and neither of us is able to submit a satisfactory explanation. We hope to be able to later.

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[28] Loc. cit.

[29] I have summarized the entire subject of the histogenesis of ossification in a paper shortly to be published, entitled, "The Relation of Angiogenesis to Ossification." In passing, the manner whereby a mass of lime is converted into bone is an interesting process, and analogous in its details to normal endochondral or membranous ossification. Furthermore, I shall show that the development of bloodvessels forms the keynote to the interpretation of the entire process.

REVIEWS

The Surgical Clinics of John B. Murphy, M.D., at Mercy Hospital, Chicago. Vol., IV; Number 1 (February, 1915); pp. 185; 41 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

This publication inaugurates its fourth year with the query by Dr. Murphy: What is an intestinal fistula? The answer is included in a diagnostic talk followed by four illustrative cases, with comments. The possible sources of intestinal fistulas are mentioned in a table three pages long. The various locations of appendicular abscesses according to the position of the appendix, are shown in seven cuts taken from Dr. Murphy's article in Keen's *Surgery*. Dr. Murphy bemoans his inability to find a term more expressive of his opinion of the "expectant treatment" for appendicitis than the *mañana* method, or *dolce far niente*.

On page 26 the intern was right and Dr. Murphy wrong about the omission from the history of the patient's knowledge of his temperature. On the next page, in speaking of end-to-end anastomosis by the suture method, Dr. Murphy refers to the "Lembert" stitch. It is probable that he meant a Dupuytren stitch, which is the one usually employed in this operation, because it takes less time for insertion.

In discussing aneurysms on page 64, Dr. Murphy is in error when he describes Hunter's treatment as "a double ligation, above and below the sac." John Hunter's method was that of proximal ligation far from the sac, as is shown by his historical ligation of the superficial femoral artery in the canal that bears his name for popliteal aneurysm, in December, 1785. With the exception of turning out the clots, Dr. Murphy's definition corresponds to the treatment of Antyllus. The second table in the book gives a classification and statistics of aneurysm.

In Dr. Mix's discussion of the case of division of the brachial plexus, he overlooks the fact that the brachialis muscle is supplied in part by the musculospiral nerve. A discussion of supraclavicular subcutaneous lesions of the brachial plexus not associated with skeletal injuries and occurring between the transverse processes and the clavicle, of which there are about twenty-one cases on record, is conspicuous by its absence, and might well have been included. We doubt that the tendons of the pectoral muscles could be cut at a point corresponding to the middle third of the clavicle.

A series of illustrations shows Dr. Murphy's technique of inserting an intramedullary splint into a fractured tibia. The open reduction of a posterior luxation of the spine at the second lumbar vertebra is particularly interesting. In discussing a case of old compound fracture of the malar bone, Dr. Murphy says: "The trifacial is chiefly the sensory nerve (of the face), although it must not be forgotten that it also contains the motor nerve supply to the masseter muscle." Why were the temporal and external and internal pterygoids not included? In discussing a case of ununited birth-fracture of the clavicle in a boy, aged nine years, the statement is made that bone transplantation is out of the question. An inlay bonegraft inserted into the anterior surface could not have been included in this assertion. A statement worth emphasizing is: "Remember that, as a rule, a Lane plate should not be used where there is a failure of union." The talk on carbuncle of the arm is very valuable. In speaking of lip carbuncles, ligation of the facial vein high up to prevent thrombophlebitis extending into the ophthalmic vein and cavernous sinus is not mentioned. The remaining cases include plastic work on thumbs, plating of a fractured femur, and gangrenous appendicitis.
P. G. S., Jr.

Arteriosclerosis: A Consideration of the Prolongation of Life and Efficiency after Forty. By Louis Faugeres Bishop, A.M., M.D., Clinical Professor of Heart and Circulatory Diseases, Fordham University School of Medicine, New York City. Pp. 383; 11 plates, and 25 figures in text. London: Oxford University Press, 1914.

This volume comes to us in the usual good dress of the Oxford medical publications. Its contents survey from every angle this disease of ever-increasing modern interest. Twenty-one chapters take up arteriosclerosis, discussing etiology, symptoms, prevention, nursing, treatment, blood-pressure, angina pectoris, life insurance, chemistry of the proteins, the prolongation of life in arteriosclerosis, and so forth. Much emphasis is laid upon protein sensitization as a cause of this malady, while the liberal protein diet is the subject of discussion in many paragraphs. The book is written in a very entertaining style. It leaves the impression that its author is perhaps a trifle overenthusiastic and that he has resorted to some unnecessary repetition in order to fill out the pages. For example, of the fifty-four pages devoted to the chapter on diet in arteriosclerosis, forty-two are devoted to cheese as an article of food. Yet the book is, on the whole, very interesting, especially so in the portions which touch upon the personal experiences of the author.

He is apparently a man who is up to date and abreast with the times. The notable feature of the work is the impressive emphasis laid upon the somewhat belated recognition by physicians that arteriosclerosis is a disease and not a lesion, that fibrosis or calcification in the arteries is not essential to its diagnosis, that such arterial changes may exist without evidence of the clinical condition whatever, and that ordinarily these vascular changes are accompanied by changes in the heart and other organs, thus frequently causing evidence of the disease entirely outside of the bloodvessels. While the book at times lags in interest, it shows all the earmarks of a thorough familiarity with the subject under discussion. It is refreshing and stimulating. It is food for thought, and seems to point in the proper direction.

T. G. S.

PRAKTIKUM DER CHIRURGIE: EIN LEITFADEN F. AERZTE UND STUDIERENDE. Von DR. D. NORDMANN, Oberärzt der 2. chirurgischen Abteilung des Auguste Viktoria-Krankenhauses Berlin-Schöneberg. 1. Teil, allgemeine Chirurgie. S. 216, mit 90 teils farbigen Abbildungen. Berlin und Wien: Urban & Schwarzenberg, 1915.

WRITTEN at the request of colleagues, Nordmann briefly presents points essential to every-day surgery, dedicating the volume to his teacher, Werner Koerte. The work is based upon his experience of many years as Assistant in the Municipal Hospital at Urban-Berlin.

In a brief introduction Nordmann sums up the qualifications of a modern surgeon, saying very properly that he must be grounded in small details, and that while he must not cling to the old too long, yet he must not be too ready to adopt the new.

In going over the book carefully the reviewer noted numerous differences in the details of surgical technique as carried out in Germany, from the American methods. Errors of omission and commission were relatively common, a few of which are subjoined.

In carcinoma of the breast, the etiological influence of a single, large trauma should be pointed out. Paget's disease of the nipple, or epithelioma of the lactiferous ducts, as well as Virchow's carcinoma mastitoides, should not have been omitted. The etiological significance of a single severe trauma in sarcoma is not mentioned. Coley's fluid is not alluded to. In pseudoleukemia the role of the diphtheroid bacillus is not annotated. In the differential diagnosis of lipoma, especially of the soft variety, cold abscess should receive its share of attention. Radium is not referred to as the best means of treating warts, nor of certain angiomata. No mention of Ludwig's angina is made throughout the book—a rather serious omission.

On the whole, the enchiridion forms a safe and reliable guide for the general practitioner who does surgery, as well as for the surgical neophyte. The medical aspect receives due prominence, and the principles of therapeutic rest, so ably inculcated by Hilton, are properly emphasized. There is a pleasing interspersion of illustrative cases throughout the volume. P. G. S., Jr.

A Text-book of Histology. By Frederick R. Bailey, A.M., M.D. Fourth revised edition; pp. 644; 384 illustrations. New York: William Wood & Co., 1915.

This is a book written for the instruction of students of normal histology, to be used in connection with laboratory work. That it has now reached its fourth edition shows that it has proved itself adapted for this purpose. The book is subdivided into four parts: Histological technique occupies forty pages, and the general account of the cell, twenty pages. The tissues are considered in eighty pages and the systems of organs in three hundred and forty pages. Over a third of this latter part is devoted to the account of the nervous system, which is written by a separate author, Dr. O. S. Strong, in a thorough manner. In each chapter, besides the description of the mature tissues, separate paragraphs are devoted to development, special technique, and general references for further study. The index is unusually complete. For illustrations, the author has adopted the easy method of selecting, with due acknowledgement, illustrations which suited his needs, from existing text-books or journals. In its present edition the book should continue to be a useful and reliable guide to the study of histology.

W. H. F. A.

A Manual of Physiology, with Practical Exercises. By G. N. Stewart, M.A., D.Sc., M.D. (Edin.), D.P.H. (Camb.). With colored plate and 467 other illustrations. Seventh edition. New York: William Wood & Co., 1914.

Authors of text-books may be divided into two groups: those who fill the pages with dogmatic statements, and those who discuss the more important problems with their reader, as it were, giving him sufficient data to exercise his own judgment, to some extent at least. Dr. Stewart certainly belongs to the latter group in spite of the fact that the book is called a manual. Only too often the sole purpose of the manual is to prepare the student for an examination. This book, on the other hand, has as its sole function the expounding of the subject of physiology in its present state of advancement. The poor or indolent student who, misled by the name, buys this book with the intention of "getting" the subject in examination form with the least possible effort will be disappointed. The subject of physiology is becoming more complex each year, and likewise each new edition of this work has become more involved. This is particularly manifest in the chapter upon internal secretions, in the discussion of the action of the pancreas, in the chapter upon respiration on the action of the respiratory centre; indeed, knotty problems are discussed with the reader in every chapter; but with a clearness of presentation and logic as to lend much interest to them. The interested student will not be repelled but fascinated. It is, indeed, a splendid book. The author possesses an exceptional tolerance for different views, but not those based upon insufficient data. This is seen when he refers to the reciprocal relation of the ductless glands, where he states, "but the premature attempts which have been made, in the absence of a sufficiency of exact data, to represent their mutual influence by crude schemata, have retarded rather than advanced our knowledge, and need not be referred to here." But one criticism can be made of this book and that is in regard to the practical exercises. They are entirely too incomplete to meet the requirements of a good medical school. E. L.

URINARY ANALYSIS AND DIAGNOSIS BY MICROSCOPIC AND CHEMICAL EXAMINATION. By LOUIS HEITZMANN, M.D. Third revised and enlarged edition. Pp. 345; 131 illustrations, mostly original. New York: William Wood & Company, 1915.

THE present edition of Heitzmann's treatise upon urinalysis conforms largely to the style and manner of presentation of the previous editions. Numerous changes have been made, however, in the text, so that the subject-matter has kept pace with the many advances made in the chemical analysis of urine, while in dealing with microscopical examination and more particularly with microscopical diagnosis, the author sets a pace which at times it is difficult to follow. Certainly if all the various types of diseases of the urinary tract could be as readily diagnosed by the examination of the centrifuged specimen as Heitzmann would have us believe, a great advance would be attained in the study of these disorders.

The book is divided into three parts dealing respectively with the chemical examination and microscopic examination of the urine and with microscopic urinary diagnosis. The first section presents admirably the various methods of chemically examining the urine which can be employed by any practitioner with only a minimal amount of apparatus. The second part is notable for the splendid drawings, illustrative of all possible organic and inorganic, normal and abnormal, constituents of the urine seen microscopically. The third division deals with the diagnosis of lesions in the urinary system, and while much that is written here is most praise-worthy, it does seem, however, that it is stretching a point to claim that practically always the diagnosis, the duration of the disease, and the prognosis can be determined by the study of the type of casts, the character of the epithelia and the other urinary constituents seen under the microscope.

The book as a whole is a commendable piece of work. It does not attempt to delve deeply into the complicated depths of urinary examination but shows clearly how much may be learned from the data obtained by the careful study of the urine in an ordinary "routine examination." J. H. M., Jr.

A Medical Dictionary for Nurses. By Amy Elizabeth Pope, Instructor in School of Nursing, St. Luke's Hospital, San Francisco, Cal. Pp. 288; 11 illustrations. New York: G. P. Putnam's Sons, 1914.

This book is of convenient size, bound in blue linen, uniform with the other books by Miss Pope. It is printed in clear type and on easily read paper. The definitions given are clear and show extensive reading and thought on the part of the author. For a dictionary of its size it is not sufficiently complete, nor is the space allotted to the various words evenly distributed. For instance, after the word *bath* there are about 1300 words; after syphilis about 300 words; whereas, many words in common use, such as, borborygmus or diverticulum, are not included. However, the definitions of the words given are clearly expressed. The work will be of value to the student nurse. M. V. S.

Die Menschliche Intelligenz und ihre Steigerung. By Dr. Med. A. Lorand. Pp. 416. Leipzig: Verlag von Dr. Werner Klinkhardt, 1914.

This is an interesting, if long, dissertation on the human intelligence and its development. Its text is divided into the various causes which have a tendency to influence thought. In the first division is discussed the influence of circulatory changes, glandular structures, the nose, climate, and general nourishment. In the second is discussed the intelligence of men and women and the influence of sex. In the third the influence of such extraneous subjects as alcohol, syphilis, migraine, and the various glandular diseases, as myxedema, etc. In the fourth the influence of sun, heat, cold, and various hygienic measures. In the fifth chapter is taken up the discussion of rational thinking, its development, and particularly the method of its improvement. In the sixth is discussed memory and its systematic development, and in the next chapter rational mental work, in which there is an interesting discussion on the influence of parents on children and the method of studying children. Perhaps the eighth chapter is most interesting, for it takes up the method to be employed in the development of intelligence in children, and the last chapter is very constructive, it being concerned with hygienic measures to be adopted in various schools to obtain the best results.

As can be readily seen from the above skeleton it would be difficult to adequately review such a work as this. To anyone who is interested in the development of intelligence this book offers a great deal. To those who do not believe that all sickly children should be done away with, this book offers some hope, for it is interesting to learn that James Watt was so ill as a child that he was compelled to sit in the house and read most of the time. That Descartes was compelled to lie in bed for eleven hours, and thus began his philosophy. That Kant, Locke, Francis Bacon, Newton, and Pope were sickly while youngsters. That Haemholtz was a hydrocephalic child and Rousseau's birth cost his mother's life. Rosseau and Voltaire were neurasthenic. The author also makes the interesting statement that those writers whose work was fantastical were very large meat eaters. He quotes Dumas the elder and Victor Hugo as shining examples of this. It is interesting also that these sickly children lived to an old age, for Humboldt died at ninety, Kant at eighty, Newton at eighty-four, Locke at seventy-one, etc. It can be seen from this that this work makes interesting reading. T. H. W.

FEEBLE-MINDEDNESS: ITS CAUSES AND CONSEQUENCES. By HENRY HERBERT GODDARD, Director of the Research Laboratory of the Training School for Feeble-minded Boys and Girls, at Vineland, N. J. Pp. 599; illustrated. New York: MacMillan Co., 1914.

THIS book represents the work done in the Vineland Research Laboratory during the past five years, it being an attempt to discover the causes of feeble-mindedness. The histories of 327 cases are presented. It is only necessary to say each case was thoroughly worked up, the material having been selected, and as a consequence the conclusions drawn merit all the attention that can be given to them. Most of the book is taken up with the detail of these histories, they being arranged as much as possible, according to whether or not the causes are probably hereditary, with neuropathic history, accident cases, those to which there was no assignable cause, and those which were unclassified.

The most interesting part of the work, of course, is that which concerns itself with the causes and theories of feeble-mindedness and the remedies. The most interesting fact brought out was that the chief cause is hereditary, 54 per cent. of the cases studied being included in this class, and in addition 11.3 per cent. being grouped under the probably hereditary class. Their conclusions regarding alcoholism were surprising. They consider only the drunkards. They conclude that alcoholism itself probably does not cause feeble-mindedness. This is contrary to the usually accepted view. They come to the conclusion that feeble-mindedness is hereditary, and that a child will at maturity have the average intelligence that its parents had, and that the inheritance of feeble-mindedness is in accordance with the well-known Mendelian law. They are not by any means certain of this, but their studies have forced them more or less to this conclusion. Only a small part of the book is taken up with practical applications. They point out what has so often been pointed out by others, that the State should recognize that paupers, criminals, and ne'er-do-wells are such chiefly because they are feeble-minded and that they should be treated as such. They deplore the fact that all the States do not take into consideration the training of such classes, but treat them as criminals, thereby only propagating this class and not really coming to any definite conclusion.

On the whole, this book is an excellent study of feeble-mindedness, and should be recommended to all physicians and laymen who are interested in this subject. T. H. W.

DEFECTIVE OCULAR MOVEMENTS AND THEIR DIAGNOSIS. By E. and M. LANDOLT, (Paris). Translated by ALFRED ROEMMELE, M.B., CH.B., and ELMORE W. BREWERTON, F.R.C.S. Pp. 99; 27 illustrations. London: Henry Frowde, Oxford University Press, Hodder & Stoughton, Warwick Square, E. C., 1914.

THIS small volume is based upon the data of anatomy, physiology, and pathology of the muscles, nerves, and centres. We miss some of the clearness we are accustomed to find in the writings of the elder Landolt. This is due to the condensation of so comprehensive a subject when dealt with in this way. It is not easy reading, but is an excellent *vade mecum* for a student who has a fair knowledge of the anatomy of the nerves and centres governing the ocular muscles. T. B. S.

LES PREJUGES EN ART DENTAIRE (PREJUDICES FOUND IN DENTAL PRACTICE). By DR. E. CHAREZIEUX, Director de l'Ecole Pratique de Stomatologie ou des Hautes Etudes Dentaires de Paris. Pp. 120. Paris: A. Maloine.

THIS is one of a series of small volumes dealing with certain fallacious ideas that have crept into the practice of various specialties of medicine. It deals with prejudices existing both in the minds of the dental profession and of the laity. The writer gives his views upon the use of local anesthetics, when a tooth should or should not be extracted, the relation of dental sepsis to general health, etc. It would seem that some of the prejudices to which attention is called are more imaginary than real, at least as applied to the dental profession in this country, where the people as a whole also are probably better educated as to the care of the teeth than in France. R. H. I.

BEHANDLUNG KOSMETISCHER HAUTLEIDEN (SCHÖNHEITSFEHLER). By DR. S. JESSNER; Sanitätsrat. Third Edition. Pp. 159; 11 illustrations. Würzburg: von Curt Kabitzsch, 1914.

THE writer takes up a considerable number of dermatological conditions in his compact little volume—"Treatment of the Cosmetic Skin Diseases." Jessner first refers to the changes in the integument that are found in the newborn; the so-called "mother's-marks," vascular and pigmented nevi, and also ichthyosis. Then the various other cosmetic skin diseases are discussed. The "snow" treatment, electrolysis, the galvanocautery, the Paquelin cautery, the Finsen light, the uviol lamp (Schott), the quartz lamp (Kromayer) are mentioned in reference to some of the various conditions. Various acids, mitin paste, and a considerable number of local applications are exploited. F. C. K.

SCROFULOSIS. By PROF. DR. G. CORNET, Berlin and Reichenhall. Translated from the Second German Edition, by J. E. BULLOCK, M.D. Second Edition. Pp. 515. New York: William Wood & Co., 1914.

THIS the second edition of *Scrofulosis* appears seven years after the exhaustion of the first edition. Such unusual delay makes the book indeed practically a new one in significance, as many previous observations have been placed on firmer ground and the opportunity has arisen for the addition of much new material. By its means a speedy grasping of this voluminous subject is made possible.

We are shown that scrofulosis is the result of a local diathesis affecting principally the skin, mucous membranes, their immediately underlying tissues and afferent lymph paths (rather than a general diathesis) upon which an infection is implanted. The infection may be tuberculous, human or bovine in origin, or due to the pus cocci. The characteristics and prognosis of the various types are described and their relation to general and pulmonary infection shown.

Therapeusis in all its aspects receives generous space. On completion of the book one feels that he has at last a rational basis for his advance in this much befogged field. The exhaustive bibliography deserves mention. A. A. H.

An Elementary Study of the Brain. By Eben W. Fiske, A.M., M.D. Pp. 132; Illustrated. New York: The Macmillan, Co.

The purpose of this small volume is to supply a simple laboratory manual for the student beginning a study of the brain.

It contains several good features. The subject is treated from the biological standpoint, the first few chapters being devoted to phylogency and ontogeny. An attempt is made throughout the work to show the physiological and psychological aspects of the various parts described. S. L.

Aids to Tropical Hygiene. By Major R. J. Blackham, D.P.H. (Lond.), R.A.M.C. Pp. 187. New York: William Wood & Co.

That wonders in sanitation have been accomplished in Panama and other tropical localities is common knowledge, but except in the vaguest way, just how this has been done is not generally known.

In this book the problem of making a tropical country habitable for white men is taken up and the solution evolved.

Such topics as water supply, food, clothing, insects and disease, animal parasites, prevention of malaria, as applicable to tropical climes will commend themselves at once to one planning a sojourn in this part of the world.

Indeed, in no way, so quickly as by familiarizing one's self with this little work, can the stay-at-home become informed on a topic of such general interest. A. A. H.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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On the So-called Granular Form of the Tubercle Bacillus.—G. BRÜCKNER (*Ztschr. f. klin. Med.*, 1914, lxxx, 360) has taken up the study of the non-acid-fast, so-called granular form of the tubercle bacillus as described by Much. As a result of his study, he concludes that the modified Gram's stain for the demonstration of the Much's granules in the sputum is unreliable for the diagnosis of tuberculosis. This applies not only to the smeared sputum, but also to antiformin preparations. Groups of granules arranged in rod form are to be looked upon as tubercle bacilli in the sputum, but these in the author's experience are found in sputa only when acid-fast tubercle bacilli are demonstrable. The author considers the granules as nothing more than tubercle bacilli demonstrable by the modified Gram's stain. They do not represent a special form of the tubercle bacillus.

An Experimental Study of the Relation of the Ductless Glands to Purin Metabolism.—FLEISCHMANN and SALECKER (*Ztschr. f. klin. Med.*, 1914, lxxx, 456), in attempting to shed light on the still obscure problem of gout, have made an experimental study in the dog of the effect of the glands of internal secretion on purin metabolism. They give extensive protocols of their experiments, only their conclusions can be given here. Nucleinic acid fed to dogs is excreted almost quantitatively. This condition is changed when pituitrin is administered at the same time, resulting in a decrease and retardation of the excretion of allantoin. When pituitrin is injected into an animal which has been placed on a purin-free diet, there frequently occurs a slight increase in the excretion of allantoin with a subsequent drop. In a fasting dog, however, this increase is missed. Adrenalin, when injected in fairly large doses, produces a marked increase in excretion of allantoin without increase in total nitrogen. The reverse effect is observed after injection of phloridzin; the total N is increased but there is no change in allantoin. In thyroidectomized animals nucleinic acid which is fed is excreted in lessened amount. Likewise under the influence of iodothyrin, there is a diminished excretion of allantoin which coincides with the marked protein destruction. Administration of paraglandol (parathyroid gland substance) has had no certain effect on purin metabolism. Purin bases fed to fasting animals are appareatly partly retained. An excess of fluid causes a marked rise in allantoin excretion.

Studies of the Blood in Variola and Vaccinia.—M. Schatzmann (*Ztschr. f. klin. Med.*, 1914, lxxx, 333) has made careful studies of the blood in seven cases of variola, two of which were fatal, and also in vaccinia. In the incubation stage of variola, the author finds a polynuclear leukocytosis. As the eruption begins to appear and as long as it remains papular, the white count is normal or subnormal. With the appearance of the vesicular stage, the white count again increases, leading to a more or less marked leukocytosis, due chiefly to increase in lymphocytes. A relative lymphocytosis persists for weeks. A marked increase of the polynuclear neutrophile cells indicates a complication. During convalescence, the eosinophiles which never completely disappear increase in number. In severe cases Türck's irritation forms, myelocytes and erythroblasts are found. A considerable number of myelocytes and erythroblasts with only a slight leukocytosis is an unfavorable sign. The persistent lymphocytosis is of some value for a retrospective diagnosis in epidemics. During vaccinia, there is a moderate increase of the white count the first day following the inoculation. By the time the local and constitutional symptoms have reached their heighth (seventh to tenth day) the leukocyte count falls, at times to normal. Then there ensues a second rise in count. The primary leukocytosis is a polynuclear, the secondary a lymphocytic. Here, too, usually during the second week, Türck's irritation forms and myelocytes are present in small number for a day or so. Finally, there may be a slight increase in the eosinophiles. There is thus a striking similarity in the leukocyte picture of variola and vaccinia, suggesting their identity.

A Study of Protein Metabolism in Experimental Pancreatic Diabetes.—A. Galambos and B. Tausz (*Ztschr. f. klin. Med.*, 1914, lxxx, 381) in a previous communication showed, contrary to the generally accepted view of the time, that hyperaminosuria occurs not exclusively in cases with impaired liver function, but also in cases of disturbance of the internal secretion of the pancreas (diabetes). Indeed, the most extreme grade of hyperaminosuria they encountered (17 per cent.) was in a diabetic with acidosis. In mild cases of diabetes on the other hand, normal values for amino-acids in the urine may be found. In diseases with increased protein catabolism such as cancer, leukemia, most febrile infections, there is a tendency to a more or less marked hyperaminosuria though it is not constant. Their clinical findings, the authors have attempted to reproduce experimentally. They reason that if hyperaminosuria occurred after complete removal of the pancreas but was absent after ligation of the pancreatic duct, this would practically prove that the determining factor was the internal secretion of the pancreas. The experiments, therefore, were conducted on this basis. Dogs were used. They were placed on a standard diet and the ammonia, total nitrogen and amino-acids of the urine were determined during a control period of three to eight days before the animals were operated upon. The authors found that the results conformed to what they expected. The catabolism of protein to its normal end products requires the internal secretion of the pancreas. An insufficiency of this secretion leads to hyperaminosuria. Pancreatic glycosuria and hyperaminosuria, they look upon as analogous phenomena. Diseases of the liver and acute infections may be accompanied by hyperaminosuria, just as alimentary hyperglycemia or glycosuria may be associated with them. It is possible that both metabolic anomalies have a common cause, and it is quite possible that this is to be sought in a decrease or loss of the internal secretion of the pancreas.

On the Vaccine Treatment of Typhoid Fever.—A. V. KORANYI (*Wien. klin. Wchnschr.*, 1915, xxviii, 85) has recently treated a small series of typhoid fever patients with Ichikawa's vaccine with such good results that he considers a report advisable. The vaccine was prepared after the method of Ichikawa. Ten loopfuls (oese) of typhoid bacilli were added to 10 c.c. of serum from a convalescent, incubated five to six hours, washed and then shaken in 100 c.c. normal salt solution containing 0.3 per cent. phenol. Experiments showed that 0.4 to 0.5 c.c. of this preparation is the proper dose. After establishing this point, the author treated twenty-four cases of typhoid fever with the vaccine. No deaths occurred. Following vaccination, a more or less severe reaction occurred, chill, rapid rise of temperature, followed by a fall almost to normal or even subnormal, with free perspiration. The reaction was very well borne. The further course of the disease may be divided into four groupings: (1) critical fall of temperature with recovery (seven cases); (2) a fall of temperature by short lysis (three cases); (3) marked improvement (seven cases); (4) no appreciable betterment (seven cases). The earlier in the disease the vaccine is given the better appear to be the results. Recurrence may follow abortive cure, but it also yields to vaccination.

Comparative Determination of Blood Sugar by Polarization and Reduction Methods.—C. MAASE and H. TACHAU (*Ztschr. f. klin. Med.*, 1914, lxxxi, 1) report the results of a comparative study of determination of blood sugar by polarization, by copper reduction (Bertrand) and by silver reduction (Tachau). In twelve cases examined, including three of diabetes, the results of the three methods were practically the same, excepting in one case of diabetes where the polariscopic readings were considerably higher than those obtained by the reduction tests. The reason for the difference, the authors were unable to determine. On the whole the polariscope gave results a trifle higher than the reduction methods; Tachau's method usually gave a slightly higher result than Bertrand's. Interesting results are reported after the administration of 100 grams of levulose. As would be expected, the polariscopic readings were increased, reduction decreased. Using the specific polarization and reduction values for dextrose and levulose, the authors calculate the amount of sugar in the blood. Levulose was highest in a patient with jaundice.

On the Treatment of Delirium Tremens with Veronal.—E. von der Porten (*Deutsch. med. Wchnschr.*, 1915, xli, 34) warmly recommends veronal in the treatment of delirium tremens. During the years 1910 to 1913, he has treated 382 cases of delirium tremens with veronal; the mortality was 5.49 per cent. The veronal was given dissolved in warm tea. On admission the patient receives 1.0 gm., and one to two hours later a second similar dose is given. If this does not suffice to quiet the patient, another gram is given five hours after the first dose. In very resistant cases a further dose may be required within the first twelve hours.

SURGERY

UNDER THE CHARGE OF

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Typhoid Spine.—Carnett (*Ann. Surg.*, 1915, lxi, 456) says that over one hundred cases of typhoid spine have been reported since the publication of the first paper by Gibney, in 1889, but less than thirty cases in which Roentgen-ray pictures were taken, and in some of these the roentgenograms were negative. To this list he added three personal cases in which the Roentgen rays disclosed definite bone changes, and says that sufficient evidence has been accumulated to prove definitely that Gibney was correct in his original view that an inflammatory organic lesion does occur in these cases. The cases which only simulate typhoid spine, whether because of neurosis, toxemia, or any other cause, but which do not present organic changes, should henceforth be excluded from the list of true typhoid spine cases. A negative roentgenogram does not disprove the presence of an organic lesion. It has been found that fully 85 per cent. of the cases occur in males, that it is most common between twenty and twenty-five years of age, and occurs as commonly in mild cases of typhoid fever as in severe ones. The vast majority of cases occur in the lumbar spine or in it and the immediately adjacent thoracic and sacral vertebræ. Commonly only two adjacent vertebræ are involved, though, rarely, several may be. Fraenkel found typhoid bacilli more frequently in the lumbar vertebræ, probably, because of the larger amount of bone marrow in them. The lumbar spine is also normally subject to greater stress and strains than the remainder of the spinal column. Typhoid spine is almost never fatal, hence post-mortem study of recent cases is wanting. The onset of symptoms was usually gradual, but in many was abrupt and acute, occurring in a few cases during the febrile period, most often during convalescence, and quite frequently some weeks or months, in one case four years, after recovery from typhoid fever. The Widal tests, when taken, have been positive. Pain over the spine has been the most constant and positive symptom, as well as usually the first to attract attention. The local pain, however, has sometimes been shadowed by the greater intensity of the referred pains. Local pain is aggravated by movements or jarring of the spine and local tenderness can be elicited and the spine is rigid in all cases, in only three or four cases did suppuration result requiring incision. The Roentgen-ray in the later stages affords the best proof of a local lesion. The great majority of the patients experienced severe or even excruciating radiating pains, especially on movements of the spine. The best form of treatment is to place the spine at as near absolute rest as possible. This may be accomplished by either plaster-of-Paris cast, spinal brace, or by continuous traction from head and feet. Pain often has ceased abruptly after fixation of the spine. Excessive pain can be relieved by the local application of heat, by aspirin or sedatives, but often opiates will be needed. Elimination should be pushed to combat the toxemia. In prolonged cases vaccines may be of service.

Tuberculosis of the Knee-joint in Childhood.—Sever and Fiske (*Amer. Jour. Orthop. Surg.*, 1915, xii, 597) studied a series of 638 cases admitted to the Orthopedic Department of the Children's Hospital, in Boston, from 1880 to 1910. The object of this investigation has been to furnish some general statistics, based on this large number of cases, to report as far as possible the varying symptoms, pathology, etc., that were met with, and to record the results of treatment under the different methods employed, as they applied to different conditions and groups. It was found that the males predominate and the right and left knees are equally affected. Trauma occurs in 30 per cent., tuberculous family history in 13.5 per cent., involvement of other joints 11.3 per cent., in order of frequency the hip, spine, ankle, elbow and wrist. Predominant symptoms occur in the following order of frequency: swelling, limitation of motion, flexion, heat, pain, subluxation, abscess, sinus, fluid, knock-knee, and outward rotation. Abscess occurred in 27 per cent. of all cases. Osteal involvement predominates in children, but synovial disease is found frequently with it. Disease of tibia alone is rare, involvement of tibia and femur together is commonest, of femur alone is next. Bony enlargement is commonest in femur alone, and in the internal condyle. Treatment was by traction, plaster, splint, and operation. Thirty-five per cent. were operated upon, the relative frequency of the operations being forcible correction, incision and drainage, osteotomy, tenotomy, excision, arthrotomy, aspiration and amputation. The first four types of operation had to be repeated in many cases. The average duration of treatment was 4.9 years, cases not operated on averaging 4.2 years, those operated averaging 5.8 years. The results of treatment of 251 of these cases of three years or more duration under treatment show that about 65 per cent. had satisfactory results, 35 per cent. unsatisfactory, the oldest cases showing the best results, healing and ankylosis increasing with duration of the lesion. Although the cases operated on undoubtedly represent the severest types, it is significant that much better results were obtained in the non-operated cases, one-quarter of the latter as compared with one-half of the former having undesirable results. Forcible correction and excision were the only operations in which more favorable than unfavorable results were recorded. Outside of the few probably favorable cases which received splint treatment only, the best results in the non-operated cases were obtained by the combined splint and plaster treatment, if the healed cases be taken as a criterion, otherwise there is little choice in the method of treatment. The results of those cases which were in the worst condition at admission, as represented by the groups which were put in traction, or had abscesses, compare unfavorably with the general average, showing a predominance of unsatisfactory results and many unhealed cases. The results of those cases of abscesses not operated are, however, far better than those which were opened.

Tuberculosis of the Hip, an Analysis of Twenty-five Selected Cases. —ALLISON (*Amer. Jour. Orthop. Surg.*, 1915, xii, 623) says that these cases were treated at the Saint Louis Children's Hospital within the last four years, and have gone on to recovery in that they have ceased to have symptoms and have weight-bearing joints. The analysis of these cases is intended to demonstrate the value of the Bradford traction-abduction splint in the routine treatment in the ambulatory stage of hip-disease. In view of the fact that the extent of the ankylosing process is dependent upon the intensity of the disease process and the amount of destruction of the joint cartilage, it is very essential to protect the hip-joint both from weight and from motion in the acute stages of the disease, and during the convalescent stage traction properly applied is a most important element in successful treatment. Allison is not of the opinion that an ankylosed joint is the best result that can be obtained in hip-disease, and he feels that what Lorenz calls the "weight-bearing therapy" is an incomplete and careless manner of treatment. He has gained from the cases studied the following facts: The average shortening where plaster-of-Paris spicas were used was 1.45 inches; where the Bradford traction-abduction splint was used it was 0.56 of an inch. Where plaster-of-Paris spicas were used the average atrophy of the thigh was 1.47 inches, and of the calf ½ inch; where the Bradford traction-abduction splint was used the average atrophy of the thigh was 1.27 inches and of the calf 0.76 of an inch. The use of traction, therefore, does not materially increase the amount of atrophy. Motion was preserved to all the hip-joints treated with traction-abduction splint and was lost in 60 per cent. of the cases treated with plaster-of-Paris spicas. Abscesses have occurred in 33 per cent. of the cases treated with plaster-of-Paris spicas, and in 40 per cent. of the cases treated with traction-abduction splints. Of the cases treated with plaster-of-Paris spicas there were six cases that developed complete bony ankylosis. In five cases it was necessary to do an osteotomy of the femur in order to correct adduction and flexion deformity. Two of the cases recovered with free motion in all directions; two recovered with motion through 45 degrees in flexion. Of the cases treated with Bradford traction-abduction splint no case resulted in bony ankylosis, and in no case was it necessary to correct deformity by osteotomy. All the hips were held in position of abduction.

THERAPEUTICS

UNDER THE CHARGE OF

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An Experimental Study of Methods of Prophylactic Immunization Against Typhoid Fever.—GAY and CLAYPOLE (*Arch. Int. Med.*, 1914, xiv, 67) review the history of the development of artificial immunization against the typhoid bacillus in animals and human beings and discuss some of the many preparations of the typhoid bacillus used for this purpose. Particular attention is drawn to the reputed advantages of living sensitized typhoid vaccine (Besredka) as opposed to other types of vaccine. The many vaccinns that are still being advocated indicate that the best vaccine has not yet been found and that the best method of proving which is the best vaccine has not yet been determined. Sensitized cultures of the typhoid bacillus, whether whole or as sediment, produce little or no reaction in human beings with the possible exception of those who have previously suffered from typhoid or those who have been immunized. By comparing their results with those of certain other observers, the authors conclude that a considerable degree of reaction, both local and general, is avoided by the use of these sensitized cultures, which possess the further advantage, so far as their experimental work can determine, of producing a more durable type of immunity. Gay and Claypole recommend vaccination at short intervals (two days) in human beings, which is rendered quite possible with the mild vaccine they employ, and is evidenced from animal experimentation, as giving rise to less toxic effect and to fully as durable an immunity as vaccination at longer intervals. This type of vaccination has the further advantage of completing the prophylactic treatment of three injections within a week. They further believe that a polyvalent vaccine derived from strains of the typhoid bacillus isolated in the vicinity of patients who are to be treated is advantageous, judging largely from the work of other observers. A further advantage in the use of sensitized cultures is that a polyvalent vaccine, no matter how recently the strains may have been isolated, is also almost entirely free from untoward effect. They recommend for prophylactic immunization against typhoid, three injections of the sediment of a dried, ground, sensitized culture of several local strains of the typhoid bacillus mixed together, given at two-day intervals and in a dosage of $\frac{3}{32}$ mg. of the original dried culture, which corresponds, as has been determined, to a dosage of approximately 750 million living typhoid bacilli. Gay and Claypole state that their experimental and clinical results as well as the work of many other investigators lead them to believe that the agglutinating power of the serum is by no means indicative of the degree of protection afforded against infection with the typhoid bacillus. They believe that the skin test with the typhoidin solution is of far more prognostic value. They state that persons immunized with various types of typhoid vaccines react in the majority of cases for about two years and then become more frequently negative. The authors regard a negative skin test after vaccination as an indication for revaccination.

A Clinical and Bacteriological Study of Hexamethylenamin as a Urinary Antiseptic.—Levy and Strauss (*Arch. Int. Med.*, 1914, xiv, 730), in an endeavor to ascertain the value of hexamethylenamin as a urinary antiseptic, examined the urines from 91 patients receiving this drug. Most of the urines were examined twice and some of them as many as six times. The 91 cases may be divided as follows: surgical 42, medical 32, and genito-urinary 17. The urines of all of the 91 patients gave a test for formaldehyd varying from 1 to 20,000 to 1 to 5000. The urines from 72 patients showed the presence of formaldehyd in the strength of 1 to 10,000. They conclude that in almost all cases hexamethylenamin is excreted into the bladder unaltered and thin, under the influence of the acid in the urine and the warmth of the body, is broken down into formaldehyde. They believe that in those cases in which formaldehyd is liberated in the kidneys it is probably due to the higher than normal acidity of the urine in the kidneys. These are undoubtedly the cases that develop a hematuria or albuminuria. The authors tried the effect of hexamethylenamin in a 10 per cent. neutral solution and found that it had neither bactericidal or inhibitory influences upon bacterial growth. They found that formaldehyd to be of value as a urinary antiseptic must be liberated in strengths varying from 1 to 15,000 to 1 to 5000 depending on the organism the growth of which is to be inhibited. To be of bacteridical value it must be liberated in strengths from 1 to 5000 to 1 to 1000, also depending on the organism. They determined the concentration of formaldehyd in the urines examined by the Rimini method which gives only an approximate estimation. By this method they never demonstrated formaldehyd in a concentration greater than 1 to 5000. Hence they believe it reasonable to assume that formaldehyd is never present in urine in solution strong enough to destroy any organism except the bacillus typhosus. However, it may exert an inhibitory action on other organisms. They found that a high acidity is necessary for the destruction or inhibition of organisms other than the typhoid bacillus. This high acidity in combination with the formaldehyd may produce injury to the kidney tissue. The final conclusion of the authors is that hexamethylenamin appears most efficacious as a prophylactic during the course of typhoid fever for the prevention of pyelitis or cystitis. Its successful use in this connection has been demonstrated both clinically and bacteriologically.

Mouth Infection as a Source of Systemic Disease.—Billings (*Jour. Amer. Med. Assoc.*, 1914, xliii, 2024) confines his remarks to alveolar infection of the jaws as related to systemic disease. Chronic arthritis has been especially studied, and in order to make a proper diagnosis of the cause of the disease radiographic films of the jaw must be made. Alveolar infection and root abscesses may be primary and due to unhygienic conditions of the mouth, but Billings believes that irrational dentistry—teeth with infected pulp, crowned or improperly filled—prolongs and intensifies the infection. The chief systemic diseases induced by such infection are malignant endocarditis, chronic arthritis, and myositis. Cultures were made from the infected alveoli and tooth sockets. The dominant organisms found belong to the streptococccus-pneumococcus group. In addition staphylococci, a fusiform bacillus, the Bacillus aërogenes capsulatus, and various saprophytic organisms were found. In five patients suffering from Hodgkin's disease, an alveolar abscess has culturally yielded the diphtheroid bacillus, which is found in the enlarged lymph nodes in that disease. After removal of the source of the infection the attempt should be made to increase the defences of the body against the systemic infection. Autogenous vaccines may be used to assist the body in overcoming the systemic infection but should be considered only as aids in the treatment. General hygienic and tonic measures to increase the resistance of the patient are essential. The treatment of chronic joint affections is long and tedious and must be supplemented by graduated passive and active exercise and other measures to improve the local circulation in the joints involved.

The Vaccine Treatment of Typhoid.—V. Koranyi (*Wien. klin. Wchnschr.*, 1915, xxviii, 85) reports a series of cases of typhoid which were treated by Schikawa's serum. This serum is, briefly, a mixture of typhoid bacilli and serum from typhoid convalescents. The details of the preparation of the serum are not given in this article. In all, 24 cases were treated with no mortality. A considerable reaction, as a rule, followed the injection of the serum usually in the form of chills and a rise of temperature followed by a sudden fall. The fall in temperature was so marked that at times the temperature became subnormal. He divides the cases treated into four groups: First, those that make an unevently recovery with, as a rule, a critical fall in temperature. The second group includes those cases in which the temperature rises moderately after the injection of serum and then comes down by lysis in a few days. The third group comprises those cases in which after a sharp rise in temperature there is a sudden and decided improvement in the clinical symptoms. The fourth group includes those cases that did not seem to be influenced favorably or otherwise by the injection of the vaccine. V. Koranyi says that it cannot be definitely determined whether a revaccination would not help after the primary vaccination failed. He believes that some cases of typhoid fever can be aborted by means of this vaccine. The first week of the disease is the best time for successful treatment. He adds that cases that have been aborted and subsequently recur usually respond the second time to the abortive treatment.

The Present Status of the Crotalin Treatment of Epilepsy.—Thom (*Boston Med. and Surg. Jour.*, 1914, clxxi, 933) opposes the foundation upon which the crotalin treatment of epilepsy is based; namely, that epileptic convulsions are induced by increased coagulability of the blood and that the good effects obtained by crotalin therapy is due to its action in lessening the coagulability. Thom tested the coagulability of the blood in 203 epileptic patients free from any clinical evidence of organic brain lesions. Blood was taken for this purpose before, during, and after convulsions; 92 per cent. of these cases fell within normal limits; 5.5 per cent. was less than the minimum limit, and 2.5 per cent. over the maximum limit. Thom was convinced there was no relation between the coagulation time of the blood and convulsions in epileptics. Fourteen cases of idiopathic epilepsy were started on crotalin with the intention of continuing for three months. On three of these patients it was necessary to suspend treatment; in the first case because of the development of hysteric attacks; in the second the convulsions were so markedly increased in frequency and severity that at the patient's request treatment ceased; the third case exhibited such violent local and systemic reactions that Thom did not feel justified in continuing the injections. Of the remaining eleven cases which were kept on treatment for the three months, six became worse, that is, the convulsions were either increased in frequency and severity or some unusual mental disturbance made itself manifest; four showed no change whatsoever; and one, a typical case of hystero-epilepsy, showed improvement, undoubtedly the psychological effect of the administration rather than the drug being the cause. Thom collected a total of fifty-eight cases from Pennsylvania, Virginia, and Michigan. Six, or less than 10 per cent., showed improvement; twenty, or more than 35 per cent., became worse, and three died while treatment was being carried out. The remaining twenty-nine cases were apparently unaffected by the drug. Thom mentions among other disadvantages of applying the crotalin treatment that the remedy is frequently contaminated by anaërobic organisms and that it is impossible to obtain a standardized dosage, as pointed out by Noguchi who found that crotalin lost from 25 to 50 per cent. of its strength in the process of drying.

The Treatment of Tetanus.—Siemon (*Münch. med. Wchnschr.*, 1914, lxi, 2322) reports 26 cases of tetanus, the first 10 of which were treated with serum alone and only one recovered. Since then magnesium sulphate was used and in some cases without serum and in others combined with the serum treatment. Of 11 cases treated with serum, magnesium sulphate, and other symptomatic remedies not one was lost. He does not speak definitely of the five other cases, which may still be under treatment. He believes that the remarkable change in the mortality must have been due, in part at least, to the symptomatic use of magnesium sulphate. Narcotics were used very sparingly in the treatment of those given magnesium sulphate; a small dose of chloral was given in the evening to secure sleep, In the wounded coming under Siemon's observation the number of cases of tetanus among the Germans was about five times the number among the French. The author suggests that the higher incidence of tetanus in the German soldiers must be due to some special factor as yet unexplained.

PEDIATRICS

UNDER THE CHARGE OF

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Patent Ductus Arteriosus.—E. W. Hall (*Archives Middlesex Hospital* xxxi, 39) reports three cases of patent ductus arteriosus. The first child, aged two weeks, was attacked suddenly by cyanosis and cessation of breathing. On admission to hospital it appeared healthy. There was nothing to suggest organic disease, and no physical signs of any heart lesion were present. The child had several subsequent attacks, succumbing to one of them. Respiration ceased and cyanosis developed rapidly. The heart, however, continued to beat regularly and the pulse could be felt at the wrist. The heart sounds became inaudible toward the end of the attacks. At autopsy the only lesion found was a patent ductus arteriosus, which was large enough to allow the passage of a large probe. The second child, aged two weeks, had similar attacks. No murmurs were heard over the cardiac area, but there were signs of bronchitis in the lungs. The child died during an attack, and the patent ductus arteriosus was the only abnormality found. The third child, aged three weeks, had a similar history and had typical attacks of cyanosis with complete inhibition of respiration, requiring artificial respiration for twenty minutes and oxygen and brandy to revive it. Autopsy again showed only patent ductus arteriosus. Most cases are reported as occurring in combination with other forms of congenital heart lesions, especially pulmonary stenosis. The cyanosis is probably due to a deficient aëration of the blood. The systolic murmur heard over the cardiac area, as described in the text-books, was absent in these cases. There was also no sign of obstruction during the intervals of the attack.

Cerebellar Abscess in a Child.—Ashby (*Brit. Jour. Child. Dis.*, 1915, xii, 105) reports a case of cerebellar abscess in a child aged 4 years; in which the only symptoms were continued headache and listlessness and continued posture of lying on the right side. There was a slight bronchitis and the pulse was slow and irregular. The temperature was normal throughout and the cerebrospinal fluid was not under pressure, was clear, and normal except for a slight excess of lymphocytes and polymorphonuclears. The urine was normal and there had never been any discharge from the ears. Optic neuritis was present and became slowly worse but the pupillary reactions were normal. She was in hospital five weeks and lay in her usual position on the right side maintaining her listless attitude. For the last three weeks she vomited on an average of two or three times a day. After five weeks she had a right-sided convulsion and died. No diagnosis had been made except an improbable one of tuberculous meningitis. On autopsy a large abscess was found in the substance of the right cerebellum. The pus was creamy and contained pneumococci. The origin of the abscess is not discernible as the ears were normal. The slight bronchitis may have been the starting point. The few localizing symptoms during life were the persistent lying on the right side and the right-sided convulsion. There was no nystagmus or tendency to fall to one side more than another.

The Oculo-cardiac Reflex.—Gunson (*Brit. Jour. Child. Dis.*, 1915, xii, 97) gives the history of the investigations into the oculo-cardiac reflex and his observations of it in observations with the polygraph in cases of diphtheria and scarlet fever in children under twelve years of age. Observations made by Mackenzie on cases of acute rheumatism were similar to those made by Gunson. This reflex consists of a reflex change in the rate of the heart and often in the rhythm following ocular compression. The path of the reflex is supposed to be along the fifth cranial nerve, medulla and vagus or sometimes the sympathetic. It produces the same cardiac changes as vagus pressure in the neck. When there is no slowing, or actual quickening of the pulse the result is negative. The reflex is positive in normal persons. It is positive in 92 per cent. of children convalescent from diphtheria and scarlet fever. In 8 per cent. the reflex is negative. These are highly nervous cases. In cases of so-called cardiac paralysis the reflex is negative. In cases that recovered the reflex became positive when the heart returned to normal. Among the cardiac results obtained in positive reflexes were, slowing of the whole pulse with stoppage of the heart in some cases as long as four seconds; production of premature contractions, reduction of the a–c interval and in diphtheria cases only complete dissociation of auricles and ventricles. The oculo-cardiac reflex is apparently of no diagnostic importance unless in confirming the nervous origin of postfebrile bradycardias. Gunson claims it does not differentiate cardiac failure from myocardial lesions from that due to nervous lesions since this would presume the independence of the muscular and nervous functions of the heart.

Rupture of the Heart in a Child.—Anderson (*Lancet*, 1915, clxxxviii, 647) reports a case of rupture of the heart in a girl five years old and apparently in fair if not good health. A hematoma was found in the left ventricular wall. The cavity was filled with blood and it had ruptured externally into the pericardium. There was an extensive rupture across the inner portion of the posterior wall of the chamber and the torn area almost encircled the ventricle. There was a stenosis of the lumen of both coronary arteries and the left one was obliterated at the seat of rupture. The lymphoid tissue throughout the body was increased in amount and the liver was large and waxy in appearance. Microscopically there was shown increased fibroid tissue through the heart muscle and liver. There was thickening of the vessel walls of the heart with frequent thrombosis. While the explanation of this condition may be that of thrombosis and abnormal development of the coronary arteries, or to necrosis of the heart wall from infarction, still the probable cause, primarily, was a syphilitic endarteritis. Inherited syphilis is a frequent cause of congenital heart disease. The work of Warthin has shown the heart to be a favorite lodging place for the Spirocheta pallida, even when they were not demonstrable everywhere else in the body and that a large percentage of congenital cardiac conditions are due to this cause and lead subsequently to arteriosclerosis. In the present case a few spirochetæ were found in the heart muscle, and many in the kidney, so that with the evidences of syphilitic processes in other parts of the body the cardiac findings can be interpreted as congenital syphilitic disease.

OBSTETRICS

UNDER THE CHARGE OF

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Icterus in the Newborn as an Infectious Disease.—Pfältzer (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) reviews the reports of cases by Schmorl, Beneke, and Esch, and adds a case under his observation in the clinic at Halle. The child was the fourth of a healthy mother, whose second child was stillborn, the two others living and vigorous. There was nothing abnormal about the pregnancy, labor was spontaneous, the child was born living and cried vigorously. The effort was made to have the child nurse, and as the mother's supply was insufficient the bottle was given, but was not well taken. The child was finally fed with a spoon. On the second day after birth well-marked icterus developed. The child was apathetic and moved but little, the temperature rose at evening to 103°, and at the end of the night the child died. At autopsy, the color of the skin was both icteric and cyanotic. The toes and fingers were drawn in convulsively. The stump of umbilical cord was dry, but the tissues about the umbilicus were infiltrated. Both legs were slightly edematous. There was ecchemosis of the conjunctiva. The ears, nose and mouth showed nothing abnormal. The abdomen was soft and not especially large. The fatty tissue was not in excess, the muscular tissue dry, pale, and icteric. In the region of the umbilicus on the inner aspect there was edema; no suppuration was present, and the vein and arteries were normal. The situation of the abdominal organs was normal, and in the region of the head and face there was bleeding into the substance of both temporal muscles. In the longitudinal sinus there was dark fluid blood but none beneath the dura. At the base of the brain there was a peculiar grayish-yellow color, which became deeper in some portions. There was no especially jaundiced color in the convolution of the brain or the medulla, but some other portions were markedly jaundiced. This was especially true in the region of the optic thalamus. The same was true of the medulla oblongata. The hypophysis in its nerve fibers was a deep yellow in color. In the pericardium there was bile-stained fluid. About the tongue the tissues were jaundiced, and there were patches of necrosis on the tongue, esophagus and larynx, deeply colored. The yellow exudate simulated somewhat a diphtheritic membrane. The spleen was much enlarged, dry and dark red. The stomach was dilated and contained colorless mucus. The mucous membrane of the stomach was dark red and showed small portions stained deep yellow. This was also true in the duodenum. The mucous membrane of the bowel was somewhat thickened and dry, the liver not markedly jaundiced, the gall-bladder full of bile, the suprarenal bodies very large and grayish in color, the kidneys full of uric acid infarcts, and the urinary bladder stained a deep yellow. There was nothing of especial interest in the muscles. Microscopic examination of portions of the brain and nervous system showed the intense yellow staining of nuclei, which has given to this disease the name of nuclear jaundice, or in German, "kern icterus." Bacteriological examination of the blood was negative, although crystals of bilirubin were present. Bacilli-like staphylococci were found in great abundance in mucus taken from the esophagus. Blood from the heart, spleen and also the bile, was sterile. From the liver was obtained the Bacillus coli communis, and this germ was found in the region of the umbilicus, and also in some of the muscles. In searching for the point at which the infection gained entrance to the body, the esophagus was thought to be the point of infection. The diagnosis of nuclear jaundice, or kern icterus, with diffuse myositis resulting from infection by the B. coli communis, and staphylococci, was made. The three points of clinical interest which seem to go together, are the presence of the B. coli communis, multiple lesions in the muscles, and the changes in the nuclei in the tissues of the nervous system. As regards diagnosis during life, one must observe the presence of jaundice, and when to this is added convulsions or convulsive movements of the muscles, if the patient be an infant, the diagnosis may be provisionally made.

Fibroids of the Uterus and Twin Pregnancy.—Montuoro (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) reports the case of a multipara in the third month of pregnancy with interstitial fibroids in the uterus. It was determined not to interfere, with the hope that in some way spontaneous birth might occur. Two weeks after the patient was first seen, at the middle of the third month she had severe pain and hemorrhage, and an abortion with twin ova. Two months later hysterectomy was performed. The writer also reports the case of a multipara, aged forty-two years, who suffered from metrorrhagia and menorrhagia, for which a curetting and amputation of the stump was done. It was found that the patient had in addition a fibroid tumor of the uterus. Some years afterward she became pregnant and the fibroid tumor had considerably increased in size. A physician who was consulted attempted to produce abortion, which resulted in profuse hemorrhage which threatened the patient's life. From this she gradually recovered, and afterward became again pregnant with twins. This pregnancy terminated in sudden abortion at about the third month. After this second abortion the fibroid growth increased enormously in size, and hysterectomy was performed. The patient made a tedious recovery from the operation, having had a thrombus in a vessel in the left lower extremity. The third case reported was that of a primipara, aged thirty-one years, married five months, and pregnant about three months. She had suffered much from abdominal pain, with edema of the lower extremities and interference with the functions of the bladder. On examination, the urine contained 2 per cent of albumin. On palpating the abdomen a hard and painful tumor was found in the region of the uterus, the genital organs were bluish in color, and the cervix drawn toward the left side. The characteristic conditions of early pregnancy in the pelvis were present. A diagnosis of fibroid tumor and early pregnancy could readily be made out. The uterus was drawn considerably toward the left, and the effort was made to bring it into the direct axis of the pelvis. Abdominal section was accordingly performed and the uterus found to be within one of the broad ligaments. It was possible, however, to sever the broad ligament tissues to bring the uterus up, and perform hysterectomy. During the operation the amniotic sac was opened, and through this opening a foot of the fetus was observed. The removal of the uterus was accomplished without difficulty and the abdomen closed without drainage. When the uterus which had been removed, was examined, it was found that uterine contractions had expelled a fetus. On the following day a second fetus was also expelled. The mother made a good recovery. This case is reported to illustrate the fact that patients with fibroid tumors of any size can rarely go to full term in pregnancy. A collection of 15 cases is added, with the salient points of each. If one examines the material, from the standpoint of the statistics, we find that pregnancy proceeded normally in 28 per cent.; that abortion happened in 16 per cent.; and that surgical interference was practised in 56 per cent. The majority of operators interfere surgically so soon as it is evident that the tumor is of any size and likely to obstruct labor.

Eclampsia and Sugar in the Blood.—WIDÉN (*Monatschr. f. Geburts. u. Gynäk.*, 1915, Band xli, Heft 2) describes his investigations to determine the presence of sugar in the blood in cases of eclampsia. There is an excess of sugar in the blood during eclampsia which appears intermittently. Concerning the origin of this sugar nothing positively is known. The intoxication theory is probably the most rational. Albuminuria is not a criterion of renal intoxication, and in these cases the quantity of blood sugar varies greatly. The blood of the fetus shows no increase in blood sugar corresponding to that in the mother.

The Treatment of Placenta Previa. STRATZ (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) quotes the statistics of placenta previa as reported by different leading obstetricians of Holland, as 881 cases with a maternal mortality of 7 per cent., a fetal mortality of 43 per cent. These statistics pertain to the year 1914. In comparison with these are 236 cases treated by combined version, with a maternal mortality of 2.7 per cent., a fetal mortality of 68 per cent. His experience in the clinic at The Hague leads him to rely upon the following methods, which are available for the general practitioner in most cases: When the bleeding is not severe the patient should be put at absolute rest and narcotics given. The writer states most emphatically that in no case should the vaginal tampon be employed. Where the bleeding is severe, combined version should be performed, and the patient kept under control while the fetus is very slowly and carefully drawn into the cervix. Efforts at extraction should then cease, and the obstetrician should wait until the mother has expelled the child up to the shoulders. Delivery should not be hurried. The final extraction of the child should be done very gradually and with great care. No effort should be made to save the life of the child at the risk of the mother; and the two procedures to be avoided, in his experience, are the use of the tampon and the immediate and rapid extraction of the fetus. For cases taken to hospital, where the cervix is not dilated, delivery by Cesarean section will be advantageous.

The Cause of the High Transverse Position of the Fetal Head, Complicating Labor.—Martius (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) has studied the cases observed in the clinic at Bonn, and reports in detail illustrative cases, in some of which the successful termination of labor was brought about through the use of the Mercurio-Walcher position. In these cases the fetal head was turned transversely across the pelvic brim, and delay in labor resulted from this circumstance. In some the occiput rotated into the hollow of the sacrum while labor proceeded, while in others brow presentation developed. In seeking the causes for this condition, one must remember that the fetal back may turn in any direction during labor; on the other hand, for spontaneous birth to proceed, the head must enter the pelvis in definite relation to the pelvic diameters. These cases are observed where the contour of the pelvic brim may be described as that of a long oval, and where the fetal head also has much of this shape; also where the forces which usually produce rotation as the head passes down into the pelvis fail, as where the pelvis is completely round in shape, or the head is nearly a perfect sphere, or when the head is considerably smaller in proportion than the pelvis. The same condition pertains in cases where the head turns transversely at the brim of a normal pelvis, and the forces of rotation are abnormal; or when in flat pelvis the shape of the head, or the shape of the pelvis, prevents normal rotation. In treating this condition, the great majority of cases terminate spontaneously, in the proportion of 6 to 5, and hence the obstetrician must wait until there is no great disproportion as long as possible before interfering. External manipulation is also useless where the pelvis is contracted in the brim, or where the pelvis is almost completely round in shape. In flat pelvis, if strong version be present, normal mechanism of labor may be expected. The Mercurio-Walcher position is especially useful where there is a tendency to brow presentation, or where the greater portion of the head enters the pelvis at one side of the promontory of the sacrum. This position is the most valuable and simple expedient which we have in the treatment of these cases.

The Cause of Icterus Neonatorum.—Heynemann (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) reviews the various theories advanced regarding the causation of icterus in the newborn. In Veit's clinic in Halle he has examined the available material and finds the primary and essential cause to be deficient functional activity in the liver cells in the first days of infantile life. The circumstances which tend to produce this condition are congestion of the liver and unusually rapid disintegration of the red blood cells. The cause of the latter is not clearly known. It seems probable that one must refer it to increased activity in some of the nuclei of the liver cells.

GYNECOLOGY

UNDER THE CHARGE OF

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A Rare Type of Bladder Ulcer in Women.—Hunner (*Bost. Med. and Surg. Jour.*, 1915, clxxii, 660) reports eight cases of an unusual type of ulcer which he has encountered in women, these ulcers being characterized chiefly by their location, long duration, and resistance to all ordinary methods of treatment. His patients averaged thirty-eight years of age, while the average duration of their symptoms was no less than seventeen years. No etiologic factor could be discovered in any of the histories; three of the patients were single; the others were married and had borne children, but the occurrence of the vesical lesions seemed to have no relation to pregnancy. The ulcers, usually single, but occasionally multiple, were all located in the vertex, or free portion of the bladder, differing in this respect from the simple, solitary ulcer of Fenwick, which is found on the base, or fixed portion. In the cystoscope the ulcers appeared superficial, the granulation surface being on the same general level with the surrounding mucosa, but at operation the inflammatory process was often found to extend through the entire bladder wall, involving even the peritoneum. No deposit of urinary salts was ever seen on the ulcers. The urine in all cases was practically normal; one patient had noticed a little blood at times, but even in her urine only a very few red cells and leukocytes could be found by careful examination. All these patients had in addition to the bladder lesions a granular urethritis, with tenderness and scar tissue contraction, requiring thorough cocainization and very careful manipulation in order to perform a satisfactory cystoscopy. Hunner suggests that possibly the ulceration of the bladder and the inflammatory condition of the urethra may have some common cause, or it may be that the frequency of micturition and straining bring about a hypertrophy and hypersensitiveness of the sphincter region. The cystoscopic picture in these cases cannot be considered in any way characteristic, being merely that of any form of ulcerative condition; the diagnosis depends, therefore, on the resistance of the ulcers to all ordinary forms of treatment. The difficulty of establishing a correct diagnosis is illustrated, Hunner says, by the fact that four of the eight patients had been subjected to operations on other organs in an effort to relieve symptoms caused by the bladder condition. He advocates actual excision of the ulcerated area, after it has been definitely shown that other measures are of no avail. In five of his cases, this was carried out, with complete cure in all but one, in which it is probable that the excision was not sufficiently extensive. Of the other three cases, one has been under treatment for six years, with apparent healing on two or three occasions; the other two have been under treatment for a few months, with but very indifferent results. The operation is done through a suprapubic, extraperitoneal incision, the bladder being distended with sterile fluid or air. The line of excision should be well outside of the area of inflammation, and the edematous zone which often surrounds it, and should extend through the entire thickness of the bladder wall. The opening thus formed is immediately closed, leaving, however, a small space through which a mushroom catheter is introduced. Through this the bladder is daily washed out with silver nitrate, starting at 1 to 10,000, and gradually increasing in strength, until all traces of infection are eliminated. After removing the catheter, somewhere from the tenth to fourteenth day, the irrigations may be continued through the urethra.

Nerve Cells in the Ovary.—The study of nerve distribution in the ovary has always been beset with many difficulties, and but few satisfactory investigations have been carried out in this field. It is, however, an exceedingly interesting and important one, especially in view of the considerable role that is now being ascribed to the ovary as one of the links in the complex chain of ductless glands, whose secretions are believed to have a more or less active influence upon many of the bodily functions. In this connection, the question as to whether or not actual ganglionic elements exist in the ovary becomes of considerable interest. In discussing in this department a few months ago, Wallart's extensive investigations of the nerve supply of the ovarian substance, it was pointed out that considerable uncertainty has existed as to the presence of true ganglion cells; Wallart himself found structures which he thought must represent such cells, but could not be sure. In a still more recent publication, however, BRILL (*Arch. f. mikr. Anat.*, 1915, lxxxvi, 338) states very definitely that he has been able to demonstrate ganglion cells in ovaries of rabbits and mice, and the excellent illustrations accompanying his article seem to bear out this contention. Brill has carried out his investigations by means of the silver impregnation method of Cajal; he at first attempted to work with human ovaries, but gave these up for those of the animals mentioned above because of the greater ease of securing fresh material, and also because in rodents the internal secretory tissue of the ovary reaches a higher development, and persists longer than in man. The ganglion cells are found, says the author, in compact groups along the course of the nerve fibres, just after these have entered the ovary at the hilus; they are surrounded by a dense network of fibres, and are for the most part multipolar, with several broad-based, branching dendrits. The cell bodies are filled with a delicate network of neurofibrillæ, which converge at the exit of the axis cylinder, into which they can be followed for some distance. From the ganglion cells innumerable delicate nerves pass off to all portions of the organ, especially the follicle system, bloodvessels, and surface epithelium. In addition to the true ganglion cells, Brill found in close relation with them numerous chromaffin cells; these are slightly smaller than the ganglion cells, and do not obtain the network of neurofibrillæ. In conclusion, he states that "this vegetative nervous system of the ovary fulfils every requirement which would be demanded by the secretory function of the organ, without, however, showing any particular relation to the vasomotor innervation."

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
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Perirenal Apoplexy and Sclerosis.—As early as 1841 WILLIS described a disease of the perirenal tissues in which multiple spontaneous hemorrhages and fibroses were the chief lesions. Since then, others have made similar observations and at present some 34 cases have been reported. The pathogenesis is not clear, and LEHNERT (*Frank. Zeit. f. Path.*, 1914, xv, 268) has added another study with the suggestion as to the causative factor. The disease occurred in a man of 62 who had suffered recurrent attacks of rheumatism. Chronic valvular disease was present in the heart, while the kidneys were in a state of advanced interstitial nephritis. Associated with these, there was an unusual development of perirenal fat, throughout which many islands of hemorrhage were found. Evidence of former hemorrhage was also present while grades of inflammation could be demonstrated. It appeared that the individual had suffered repeated attacks of perirenal hemorrhages and repair. There was no evidence that the immediate lesions within the kidney had any association with blood extravasations about the capsule, nor were there any lesions in the adrenals to indicate their association in the process. It would seem that the factors bringing about the renal inflammation were also active in producing a perinephritis. The author believes that much of the hemorrhage was the result of mechanical trauma. That, however, such hemorrhage may be directly associated with the perinephritis is indicated in the report of cases in which there was not only hemorrhage in the perirenal tissues but also in the muscles and other organs.

Experimental Polyneuritis in Birds and Its Relation to Beriberi in Man.—TASAWA (*Ztschr. f. exper. Path. u. Therap.*, 1915, xvii, 27) repeated the experiments of Eijkman and others in reproducing paresis in birds by the feeding of polished rice and grain products. Others have concluded that the polyneuritis gallinarum so obtained was identical with beriberi in man. Some 200 fowl and 120 pigeons were used in these experiments. He found that when birds were fed upon polished rice and water only they suffered great emaciation and nervous debility. Motor weakness developed in about twenty days and progressed until the animals were unable to control any of the voluntary muscles. Marked degeneration of the motor nerves was demonstrated. In other instances the conditions appeared to arise through a central nervous disturbance rather than peripheral. These cases proved quite different from true beriberi. During the progress of the condition contractures and even convulsive seizures of isolated muscles were observed. The author found that when the feeding with polished rice was accompanied with other foods in moderate quantity the emaciation and anemia could be prevented but the polyneuritis would nevertheless appear. Naturally with the proper quantitative feeding these lesions may be prevented. He found that a similar neuritis can be developed by feeding cane sugar, white flour, white bread or boiled fish. The severity and character of the disease differs but very little from those induced by rice. The subcutaneous injection of rice bran was found to moderate as well as to prevent the disease. It would appear that the disease is the result of metabolic disturbances rather than an intoxication resulting from abnormal fermentation in the gastro-intestinal canal. Up to the present satisfactory results have not been obtained in experimentally producing the disease in mammalia. The results, however, obtained in birds are pathologically so similar to the muscle and nerve degenerations found in beriberi in man that the author believes conclusions can be drawn from these experiments. In animals as well as man there is an individual predisposition which permits of the development of sporadic cases among groups on a common diet.

Experimental Studies on Extirpation of Lung.—KAWAMURA (*Deutsch. Ztschr. f. Chir.*, 1914, 131, H. iii) found that dogs in which one lung has been completely removed, survive the operation and show no ill effects subsequently. It is even possible to take away some of the remaining lung tissue. The difficulty of the operation lies mainly in dealing with the stump of the main bronchus. The remaining lung undergoes a compensatory enlargement whose maximum is reached in thirty to sixty days. The empty pleural cavity on the side of extirpation is gradually filled in by a displacement of the heart and mediastinum, while the diaphragm rises considerably and the thoracic wall becomes depressed upon the side of operation. In some instances spinal curvature with its convexity toward the side of the operation develops. There are no histological changes of any note in the thoracic tissues, save evidence of compensatory emphysema with more or less hypertrophy of the pulmonary tissues.

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ORIGINAL ARTICLES

RAYNAUD'S SYNDROME: RAYNAUD'S DISEASE.

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Maurice Raynaud was a French physician, and lived from 1834 to 1881. The disease which bears his name was first described by Sir Benjamin Brodie in 1837, but was not recognized as a disease until it was described by Maurice Raynaud in 1862, under the name of "symmetrical gangrene of the extremities." The condition was not known as "Raynaud's disease" until his second article, which more fully discussed it, in 1874.

The disease or condition was first termed "local asphyxia and syncope;" it has also been termed "symmetrical gangrene." The latter name is a misnomer, as the local manifestations are as frequently unilateral as symmetrical. Raynaud's belief that the local symptoms were caused by a spasm of the capillary vessels, which shut off the circulation more or less permanently from a part, is correct. Pathological investigations have shown there is no primary disease of the walls of the vessels.

The syndrome may be defined as a condition with such vascular disturbance as to cause a more or less complete anemia or a prolonged passive hyperemia of various parts of the body, internal as well as external. No definite cause for this idiosyncrasy or peculiar instability of the bloodvessels has been discovered. There may be a local spasm of the arterioles or venules, or of both. If the arterioles are contracted the cyanotic type of congestion occurs, preceded by an anemia; if the venules are alone contracted, a hot, congested form, slightly simulating erythromelalgia, may occur.

The associated symptoms due to this bloodvessel spasm are more or less pain, coldness or iciness to the feel, numbness, later impaired function, and trophic disturbances, as shown by eczemas, small blisters, bullæ, ulcerations, suppurations or even gangrene, sloughing, and loss of the part affected. The joints of the fingers may become sore and inflamed, and ulcers often occur near the nails with deep suppuration in and around the nails. The parts affected temporarily or interchangeably during a certain period may be symmetrical, but are not necessarily so. The spasm of the bloodvessels may last minutes, hours, or days.

The simplest form of this disease is represented by cold hands or feet, or by a finger or a toe becoming stone-cold, termed "dead finger" or "dead toe." The obstruction to the circulation may attack several fingers or the whole hand, the whole foot, the nose, an ear, or there may be serious bloodvessel disturbances of the internal organs of the body. The first local symptom is coldness and anemia, with or without pain, followed perhaps by an asphyxia or a darkening of the part; and later a hyperemia may occur, with flushing and increased local circulation. In the very mild forms the local condition is similar to that of a frost-bite, with burning, itching, and later heat succeeding the coldness and anemia of the part. This symptom complex may recur and continue to recur in the same fingers or toes. There are often pigmentations, mottling, and brown spots on the skin on various parts of the body.

In a few instances recognized, and in many instances unrecognized, this syndrome is the cause of various abdominal disturbances and of disturbances of the nervous system. There may be a spasm of the retinal vessels and temporary loss of vision. There may be loss of hearing and disturbances of the senses of taste and smell from contraction of the bloodvessels. There may be loss of speech, dizziness, paralysis, psychic disturbances, epilepsy, and cataleptic symptoms from these bloodvessel disturbances. Severe, intense headaches may occur, with burning sensations of the face and head and hot flashes. The menopause symptoms show in a mild form this vasomotor instability. There may be such disturbance of the bloodvessels in the head as to give a feeling of constriction. This is the kind of headache that is complained of by some individuals.

It is possible that some forms of epilepsy without any assignable lesion may be due to this peculiar disease. At least it is interesting to note that such cases of epilepsy as have an aura may sometimes have an attack aborted by the inhalation of such a vasodilator as amyl nitrite.

Temporary loss of muscle power and sensations and momentary paralyses may be due to spasms of the bloodvessels in certain areas of the brain. Temporary or recurrent albuminuria, and even hematuria, may be caused by sudden spasms and later congestions of the renal vessels. In other words, this bloodvessel spasm is the cause of many apparently serious nervous disturbances and of many abdominal disturbances that have led to operation, and yet nothing pathological has been found. Such contractions of the bloodvessels in the abdomen generally cause pain, and may cause distention, vomiting, and symptoms simulating all kinds of colics.

Edema of the face or of one or more extremities may occur, and may suggest angioneurotic edema. There may be symmetrical swellings of the extremities in both angioneurotic edema and in Raynaud's disease. There may be paroxysms simulating malarial fever, with chills and subsequent high temperature.

The disease is not a pathological entity. It is caused, the writer believes, by disturbances of several of the internal secreting glands, especially of the thyroid and suprarenals, and also perhaps of the ovaries. The disease is frequently associated with hysteria and with disturbances of the female pelvic organs. Amenorrhea is not always a factor, but is a frequent symptom of this syndrome.

Wherever the disease has its local manifestations a vasodilator as nitroglycerin, seems to be of benefit. Whether there is too little thyroid secretion or too much suprarenal secretion, or whether there is an insufficient ovarian secretion (and thyroid extract stimulates the ovaries), certain it is the administration of thyroid extract is generally of benefit.

DIAGNOSIS. Ordinarily mild cases of this disease are not difficult to diagnose, that is, the "dead fingers" and icy cold hands and feet. Also easy of diagnosis are the severe cases in which there is gangrene of some part of an extremity, especially when it occurs in young individuals and is symmetrical. Obliterating endarteritis or advanced arteriosclerosis is likely to occur only in individuals who are old, and is more likely to occur in men than in women, and peripheral gangrene from this cause is generally readily diagnosed. Embolic obstruction of some terminal vessel, with possibly gangrene, will generally show a history of some acute disease that may cause embolism or some chronic valvular disease of the heart.

Raynaud's syndrome occurs mostly in women, and will be found associated with disturbances that are well recognized as due to disturbances of the thyroid gland. It is also frequently associated with disturbances of the menstrual function. It can occur at any age, and has even been noted in young children.

The disease which at times it may simulate is erythromelalgia. This disease is rare, and was first described by Weir Mitchell in 1872 and again in 1878. He coined the word "erythromelalgia," which means "red, painful limb." As its name implies, it attacks an extremity, is painful, and the color of the part affected is bright red. The part feels hot, and cold soothes it. It is made worse by heat. The cause of the disease is unknown, though Weir Mitchell thought it might be due to an inflammation of the nerve endings.

The disease may be transient and intermittent, or it may cause more or less incapacity. Although it may stop and may not recur, no treatment seems to have any special effect upon it. In erythromelalgia the feet are more frequently affected than the hands. The condition is worse in hot weather and better in cold weather. Sometimes there seems to be an interrelation between Raynaud's syndrome and erythromelalgia, both conditions occurring in the same patient, or at least erythromelalgic symptoms may be present in a patient who has Raynaud's syndrome.

The differential diagnosis of Raynaud's syndrome from erythromelalgia may be briefly stated as follows: Raynaud's syndrome occurs at all ages; by far the majority of cases occur in females; it is likely to be symmetrical; the disturbance is increased by cold; the part attacked is more or less anesthetic and pale, or it may be livid, and may be icy cold. On the other hand, erythromelalgia generally occurs after twenty years of age; it is more frequent in males than in females; it is almost always asymmetrical; it is benefited by cold and not increased by it; the part affected is tender instead of anesthetic; it is pink or purplish in color; it is hot and the bloodflow to the part is increased.

Syringomyelia, a disease due to a gliomatous growth in the spinal cord, presents a very different set of symptoms from Raynaud's with paralysis, muscle atrophy, and some loss of sensation. The only similarity to Raynaud's syndrome is that there may be such trophic destruction that a phalanx may be lost.

Angioneurotic edema, another trophic disturbance, needs to be mentioned in this connection, because it may occur in an individual who has Raynaud's symptoms. The treatment of angioneurotic edema is very much more satisfactory than is the treatment of either Raynaud's disease or erythromelalgia. The probable cause of angioneurotic edema is a disturbance of the sympathetic nervous system affecting the vasomotor nerves, probably due to toxins in the blood, similar to those that cause urticaria, especially giant urticaria. Such a condition is probably a sort of anaphylactic reaction.

Mild ergot poisoning may simulate Raynaud's syndrome.

To sum up the diagnostic points in Raynaud's syndrome, it should be remembered that it may be very mild; that women are attacked much more frequently than men; that the commonest age is from fifteen to thirty, though no age is exempt; that frequently uterine and ovarian disturbances will be found; that the worst attacks sometimes occur periodically, with a more or less close relationship to the menstrual epoch; and that some of the well-known symptoms of a disturbed thyroid secretion are often present, probably more frequently on the side of hypothyroidism than hyperthyroidism.

It has been repeatedly stated that no treatment is of any value in Raynaud's disease except perhaps nitroglycerin. I have found this not to be true; that treatment to stimulate a more healthy activity of the thyroid gland has been of marked benefit, especially in severe cases, such treatment being thyroid extracts and iodides. Nitroglycerin will always help the condition, and so will local hot baths. In other words, the writer believes that Raynaud's syndrome is not always incurable, and that it is due to a disturbance of the internal secretions, and probably more especially to malsecretion of the thyroid and suprarenal glands. Certain it is that treatment aimed to correct these secretions is beneficial and many times curative.

Before presenting a series of brief clinical histories of this syndrome, we wish to urge that it be recognized and never forgotten that every disease, severe in its entirety, may occur in mild forms, and "missed" cases may occur. The grades of severity of Raynaud's syndrome are as follows:

1. It may be so mild as not to be recognized. Such patients have cold hands and feet, irregular pains in various parts of the body, and they are cold in winter and hot in summer (vasomotor ataxia, as it has been termed). There may be so much contraction of the peripheral bloodvessels that the internal vessels, especially the abdominal, are dilated, and frequently diarrhea is caused, sometimes termed "intestinal sweating," from which cause a patient may have a morning diarrhea without other symptoms. Or there may be such abdominal congestion as to cause various other gastrointestinal disturbances, albuminuria, etc. This kind of congestion or spasmodic contraction of bloodvessels is probably often the cause of ovarialgias, delayed and painful menstruation, and menorrhagia.

2. There are cases of medium severity in which there are ice-cold hands and feet, chilblains of varying degrees, sore fingers and toes, suppurations around the nails, perhaps severe headaches, and there may be erythromelalgic symptoms of red face and red hands, with or without pain. There may be faintness or syncope, dizziness, some slight nervous disturbances, as of the eyes, and recurrent albuminuria or hematuria. This condition may be one of the causes of albuminuria of adolescence and of orthostatic albuminuria.

3. Severe cases, occurring less frequently, in which there may be serious heart disturbances, deep ulcerations of the fingers and toes, serious cerebral symptoms, or severe abdominal symptoms.

4. There may occur, very rarely, such serious and uncontrollable spasms of the bloodvessels as to cause gangrene and sloughing of parts of the extremities. It is also conceivable that fatal heart attacks may be caused by this syndrome.

The following clinical histories will demonstrate the varying types and varying severity of this peculiar syndrome:

Case I.—A girl, aged fifteen years, was first seen on February 3, 1915. She began a year ago to have attacks of the hands becoming icy cold and turning blue, and at the same time she feels very faint. The attacks last about twenty minutes, even with rubbing and with plunging the hands into hot water. These attacks are becoming more frequent. Her feet are always cold and her hands are generally cold, but during these attacks they are ice-cold. Menstruation began nine months ago and has been pretty regular, lasting about four days, and is normal in amount. She is a well-nourished, apparently perfectly healthy girl. Nothing abnormal was found, except that the thyroid is somewhat enlarged and presses toward the larynx, and she dislikes to have anything tight around her throat. Her voice has been a little hoarse for the last two years, and drops peculiarly, much as a boy's voice when it is changing.

Small doses of iodide did not benefit her, but thyroid extract has thus far prevented the attacks. There is no question that the thyroid gland can be enlarged and not be properly secreting or excessively secreting.

Case II.—The following is a case of the next degree of severity: This is a stenographer, aged thirty-four years, who for years has been troubled with cold hands and feet and with chilblains of all types and degrees. The last two years especially these cold fingers and ice-cold hands with sore, swollen knuckles and sore, tender fingers have been on the increase, especially in winter. For the last year there have been repeated attacks of little infections around the finger-nails, without any history of local injury whatsoever. These particular fingers have become extra cold, extra red, painful, and finally these little ulcerations appeared. There has never been any history of real blisters. She has always been well in most every respect, except that menstruation has been more or less irregular. She is also nervous at times, gets depressed, cries easily, and is subject to headaches, mostly from eye defects; but these headaches are always aggravated at these periods of depression. The thyroid gland is decidedly enlarged on the left side, and has been for the last few months. The gland becomes smaller under iodide, but she feels much better, and the gland is softer under thyroid treatment. There are absolutely no other signs of under-secretion of the thyroid and no signs of over-secretion. As this patient has only recently come under treatment, and as the weather is growing warmer, when the fingers and hands will improve from that fact alone, the results of the thyroid treatment have not yet been determined, but she certainly feels better generally under the thyroid.

Case III.—The following case represents another degree of intensity of Raynaud's syndrome: A married woman, aged thirty-seven years, has had poor circulation for years, and has weak heart turns. Her hands become numb, but not quite like falling asleep, she says. Often she sees only one-half of an object at a time. She frequently feels full-headed, has pain in the left side of the head in conjunction with more or less of a blind turn. With these blind turns she is likely to have numb hands, and she cannot use her hands for some time. The hands and feet get cold during these attacks. These blind turns occurred more frequently up to two years ago than since, and they last from three-quarters of an hour to an hour. During these attacks she does not hear well, and her mind is not clear as to what people are saying, or what she herself is about to say. Her face also sometimes gets numb, expecially around the mouth. Sometimes with these attacks she gets quite short of breath, and occasionally has pain in the region of the heart. Her eyes are not the cause of her headache; they have been carefully examined and excluded. The headaches are most likely to occur just before and during menstruation. She says she never felt as well as she did during her pregnancies. This was probably due to a normally increased thyroid secretion at these times. She gets short of breath on exertion, and has palpitation at times. She has consulted a large number of physicians for the above-described condition.

She has been married thirteen years, and has two children, the youngest six years of age. She had typhoid fever seven years ago and measles followed by pneumonia two years ago. The physical examination is practically negative. The tongue is a little trembly. The pulse is 96. The systolic blood-pressure 140. There is no history of epilepsy or fits or anything pointing toward that condition. The urine is normal. The thyroid gland seems small.

Nitroglycerin helps her, but she is better under small doses of iodide and thyroid, and has had no blind attacks since that treatment was started four months ago. This case shows a tendency to irregular spasm of the bloodvessels. How much permanent help can be given her I do not yet know.

Case IV.—The next patient is a woman, aged thirty-nine years, sent to me for treatment on account of severe pain in the left side of the head and in the back of the neck and for persistent insomnia. This patient was first seen by me in April, 1914. Three years before she had had some of this trouble which lasted four or five months. Now for the last four or five months she has had it again and very much worse the last three weeks. It occurs almost daily and sometimes is very severe. She has no nausea or vomiting with it. With this pain she flushes and gets very hot. The left side of the face burns, although both cheeks look hot and red. Sometimes she aches all over, and especially the arms and shoulders ache. Her hands tremble at times, and she has some palpitation and an intermittent pulse. During these head attacks tears stream down the left cheek. On leaning over the head aches much worse. The hands are sometimes bright red, at other times dark, almost cyanosed; they are always discolored she says. The redness of the hands disappears when they are held over her head. The feet are cold, and sometimes she has to put them into hot water to stop the discomfort.

She is married and has six children, the youngest four years old. Menstruation is regular. Some years ago she had some sort of a benign growth removed from the right side of the abdomen, and the appendix was removed at the same time. She does not know just what the growth was. She had typhoid fever twenty years ago. There is no trouble in the eyes to account for her headaches. She is well nourished, slightly over-weight, and has a pendent abdomen. All physical examinations are negative. The pulse is 84; the systolic blood-pressure 125.

Thyroid extract did not benefit her. Under good doses of nitroglycerin or sodium nitrite she soon improved greatly, and by June, 1914, two months after I first saw her, she was practically well of the condition.

I did not see her again until February of this year, when she had a little return of her headache, with flushing of the face and watering of the left eye. Her hands have been all right. She was again having insomnia, and again having an intermittent pulse. She was given 1 grain of thyroid a day, as larger doses had caused disturbance before, and nitroglycerin again. She immediately improved, and has been well ever since.

CASE V.—A young boy, aged eight years, was first seen by me in 1910. He gave a history of having had a large number of intestinal attacks, diarrheas, etc., and a history of having attacks of albuminuria. He had peculiar pigmentations on different parts of his body, and many leukodermic spots. There was no specific history. Heart, lungs, abdomen, and urine were negative at the time I saw him. He had a few enlarged cervical glands. This boy was in a miserable condition, and unfit to go to school. He had been put upon all sorts of diets, and all sorts of diagnoses had been made, both in this country and in England.

I believed the condition to be a disturbance of the internal secretions, largely a subsecretion of the thyroid, and on account of the pigmentations on his skin a disturbed secretion of the suprarenals. He was given small doses of thyroid, and rapidly and continuously improved, and soon was well. But for two or three years, whenever the treatment was long discontinued, he had a return of his symptoms, but was immediately again improved on taking thyroid. The child later was able to go to school, and has become a strong boy.

This was a form of Raynaud's syndrome with vasomotor disturbance of the bloodvessels of the abdomen, causing diarrheas and recurrent albuminuria.

CASE VI.—This patient, a married woman, aged twenty-eight years, was first seen in June, 1913. She had two children, the youngest eighteen months old and the oldest three and one-half years. With the first child she had had an acute nephritis and a slight convulsion, but the kidneys soon recovered. Four months before

I saw her she had had a nervous exhaustion attack of some kind, and was said to have had a pericarditis, and was sick four or five weeks. From the time of the birth of the first child she had had no kidney trouble, and there has never been any edema. For a long time now she has been having breathless atttacks with heart storms, the heart beating very rapidly and pounding very hard. Her hands and feet are generally cold and sometimes blue, and the lips become absolutely blue. Although she is pale at times, she is not anemic; the hemoglobin content of the blood is 100 per cent. Frequently one finger gets numb and cold, and remains so for hours; sometimes it is one toe. During these attacks she has a dull ache in the region of the heart.

Examination shows the heart to be slightly enlarged, with no murmurs, no roughness, and no friction. The systolic blood-pressure is 120. The lungs are normal and the abdomen negative. The spleen is not enlarged, and there are no enlarged glands anywhere. Her hair is of a light reddish tinge, but the pubic hair is absolutely white, and she says it has always been so. Menstruation has always been regular. The tongue is normal.

At the time the patient was seen in consultation her physician feared she might die in one of these attacks. She was very weak and was confined to her room, although not absolutely to her bed.

A diagnosis of Raynaud's syndrome was made, and she was given nitroglycerin and small doses of thyroid. She had a rapid recovery, soon having no breathlessness, and gaining weight. However, if she stopped the nitroglycerin she again became breathless and had heart distress. Also, as long as she takes the nitroglycerin her hands are not cold. The date of this observation is September 10, 1913, three months after I first saw her. From that time, September, 1913, I have occasionally seen her, but she cannot go long without either thyroid or nitroglycerin treatment, although there are months when she is well and takes no medicine. If she feels cold she has learned to take the nitroglycerin and to stop it when she feels better.

In February, 1914, she was again troubled with coldness and getting blue around the mouth, was breathless, and was having pain around the heart. She was also excessively sleepy, and said that her hands and feet puffed at times, althugh there was no real edema. All of this showed subthyroid secretion. She was given 1 grain of thyroid extract twice a day and $\frac{1}{200}$ of nitroglycerin twice a day, and she again soon improved. It was noted at this time that streaks of white were coming in the hair on her head. She says that from five years of age until she was sixteen she had brown spots on her skin on various parts of the body. Also, part of the hair on the head of one of her children, she says, was at first absolutely white, but now has gradually become light brown. All of this story shows a disturbed thyroid secretion and perhaps a disturbed suprarenal secretion, with symptoms of peripheral contraction of the bloodvessels and internal congestions, with disturbance of the heart. In other words, it is Raynaud's syndrome, and thyroid and nitroglycerin have been of marked benefit to her.

CASE VIII.—A girl, aged seventeen years, first came to me in February, 1911. She had been for two years under treatment for a peculiar mottling of the hands and feet. For four years her hands and feet had been more or less frequently excessively cold. These conditions were always worse in cold weather, but still they persisted somewhat in summertime. For the last three months she has had peculiar gastric crises, with terrible pain in the epigastric region, occurring even as frequently as once a week, associated with a chill and followed by fever. There is no nausea or vomiting and no loss of consciousness. She has had all kinds of treatments, and there have been all kinds of diagnoses. She has never had any sickness except scarlet fever and measles, and these were when she was a child. Menstruation is regular and normal. The family history is entirely negative.

Physical examination was negative in every respect; the urine and blood were also negative. She had a blister on the back of one heel, and she has had such sores on her feet frequently. Her hands were like pieces of ice, and were almost blue. She says her hands itch a great deal and perspire sometimes profusely, and the same is true of her feet even while they are icy cold. She has had blisters on both hands, off and on, more or less for four years. Sometimes these sores on her hands and feet have to be lanced, and she has had one on her heel for three months. Her legs up to her knees and her arms almost to the elbows were peculiarly mottled by dark bluish and brown spots, not ecchymotic, much as one sees when an extremity is thoroughly chilled and the blood begins again to circulate. There was no loss of sensation anywhere.

She was given nitroglycerin and thyroid extract. In a few days she had another abdominal attack, but it was milder then the previous ones. The sore on her foot soon healed and she had less perspiration of the hands and feet. She had one other attack of the abdominal pain the following month, but no severe attack, and no chill and no fever. A few blisters occasionally occurred, but she continued to improve under thyroid treatment.

In April of the same year, after two months of treatment, she had some attacks of becoming breathless and having pain in the substernal region, but the hands and feet were not nearly so cold. The heart at times was rapid, but the pulse had been over 100 from the beginning. Occasionally she had considerable pain in the left ovary, which was a neuralgia.

She continued to improve, and from July, 1911, was not seen until October, 1913, when she reported that she had been very well, though her hands were sometimes cold; but her feet did not get cold, she never had any more of the blisters and very little of the mottling, and no chills or abdominal pain. I know she has been well since, as I frequently see her on the street. In other word the improvement of the Raynaud's syndrome in this case was remarkable.

Case IX.—A girl, aged sixteen years, was first seen by me in consultation in 1905. The family history was negative, and there was nothing important in her previous history. She began to menstruate when she was fourteen, but had not menstruated at all during the last year, namely, from fifteen to sixteen. About a year before I saw her she had begun to have attacks of fever, dating from the time menstruation ceased. These fever attacks would last about nine days and recur in about three weeks. They were preceded by chills, headache, loss of appetite, pain in the abdomen, loose bowels, and insomnia. Various diagnoses had been made, such as hysteria, intestinal disturbance, typhoid fever, malarial fever, and Hodgkin's disease (on account of her having, during these attacks, an enlarged spleen and sometimes enlarged glands in the neck).

I saw the patient in one of these fever attacks. The glands of of both sides of the neck, of the axillæ, and of the groins were enlarged. The heart and lungs were normal. The spleen was enlarged to the umbilical line, the liver was normal in size, there were no pelvic symptoms, and the urine and blood were negative. With the history of these periodic attacks, in the absence of menstruation, I was sure that they were symptoms of some kind of a toxemia.

Although there were no signs of subthyroid secretion, except that she did not menstruate and had these symptoms of toxemia, she was given 5 grains of thyroid extract twice a day. In ten days she began to menstruate for the first time in over a year and had entirely recovered from all abnormal signs and symptoms.

Under intermittent thyroid medication she menstruated regularly for nearly a year, but after stopping this treatment she again ceased to menstruate, and after not menstruating for two months she again had a high temperature, the spleen was again enlarged, the glands of the neck were tender and enlarged, and the abdomen was tense and distended; in other words, there was a complete recurrence of the attacks of the year before.

I saw her again in consultation, and under thyroid treatment she again improved. In a few days the spleen and glands were less tender and smaller; she became apparently well and menstruated the next month.

She was then well until the following year, when she had an acute attack of tonsillitis, and again had some slight recurrence of the above symptoms. She was given thyroid, and in two or three days she was again normal. Four years following this she was still well and had been well. This is probably an instance of Raynaud's syndrome with abdominal congestion.

CASE X.—This patient was a man, aged thirty-six years, who had various symptoms of various kinds of nervous syphilis; but there were no symptoms, and never had been, of gumma in the spinal cord or brain and no real paralysis. He was seen in a consultation on account of some of his nervous pains, supposedly due to some other condition than the syphilis. Examination of the blood showed a strong Wassermann reaction, and he was treated with salvarsan, became well, and was able to attend to his business. Before he had received any salvarsan, while he was being treated with mercury, and also when he was supposed to be cured of his syphilis, he had several attacks of being unable to talk or think, sometimes with terrible headaches, and at these times he acted like a person under the influence of some drug. Sometimes he would suddenly drop a fork or a spoon, and would mumble in his speech, but at such times he was generally able to walk. These attacks never lasted long, he never showed any paralytic symptoms. These attacks were due to sudden spasm of some of the bloodvessels in his brain and represent a species of Raynaud's syndrome associated with syphilis. An association of Raynaud's disease with syphilis has been recorded by others. Salvarsan has apparently cured him, but of course he is likely to have some recurrences from his syphilis.

CASE XI.—This patient, a girl, aged seventeen years, was first seen in 1904. She gave a history of having had peculiar sleeping attacks from July, 1903, to April, 1904. In these attacks she would be practically comatose for two or three days. They generally occurred about once a month, but lately they had occurred twice a month. There never were any convulsions, although there were some symptoms of stiffening of the muscles. Occasionally there was a little mucous froth at the mouth. In the last attack previous to my seeing her she had slept for twelve hours. After wakening from the attack for several days she could not hear, and for some days could not see. At times she was almost blind. For a time she did not recognize her family, her own clothing, or her surroundings. She appeared hardly to breathe while in these semicomatose attacks. She took no nourishment or liquid during this time, and passed no urine, sometimes for two or three days. She began to menstruate at the age of fourteen, but the flow was irregular, and generally occurred about every five weeks. These sleeping attacks since they began, have occurred just before it was normal time for the period to appear.

Physical examination was absolutely negative, except that the thyroid gland seemed a little enlarged. At this time we did not recognize the association of Raynaud's symptoms, due to the contraction of the bloodvessels of the brain with what seemed to me like a toxemia. I did make a diagnosis of epilepsy and a cataleptic state, and gave her thyroid, believing that she needed this to combat whatever protein poisoning was in her system. The coma and cataleptic attacks entirely disappeared. She had one or two epileptic attacks, however, and later a few petit mal attacks. The menstruation became regular and on time, and the patient entirely recovered. She married in 1905, and was well until 1910, when I saw her last. There were no other symptoms in her case of subthyroid secretion, except that she did not menstruate on time, and that she had these periodic toxic attacks. I now feel sure she had Raynaud's syndrome, with the cerebral vessels affected, associated with a subthyroid secretion.

CONCLUSIONS. 1. Raynaud's disease is not a distinct entity; it is a syndrome caused by the disturbance of one or more internal secreting glands.

2. There is primarily no real disease of the bloodvessels, but the vasomotor control is so abnormally disturbed that most profound contraction of certain bloodvessels may occur in different parts of the body, perhaps more or less coincident with abnormal dilatation of other bloodvessels. If the contracted bloodvessels are peripheral the parts more or less lose their function and show various trophic disturbances.

3. This bloodvessel spasm may occur in the internal organs of the body as well as peripherally, though much less frequently and more difficult of diagnosis.

4. The syndrome is probably due to disturbances of more than one of the ductless glands of the body that have internal secretion, but there is always apparently some disturbance of the thyroid gland, perhaps a diminution of the vasodilator stuff of this gland.

5. Judiciously applied, thyroid treatment improves the majority of cases, perhaps all, and cures some cases. Nitroglycerin is always of temporary benefit and local heat is always of immediate benefit.

OBSERVATIONS ON A CASE OF FAMILY PERIODIC PARALYSIS.

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We have to report some observations upon a case of family periodic paralysis. The case was studied very carefully, from a neurological point of view, by Taylor[1] in 1898. The present investigations lie entirely in the field of chemical pathology.

The literature on the subject was very completely reviewed up to 1898 in Taylor's paper.

In 1901 Singer[2] gave a critical digest of the literature up to that date, with bibliography. Fairly complete bibliographies will also be found in the papers of Kramer, 1908,[3] and Gatti, 1911.[4]

Kramer counted 78 cases in the entire literature, and since that time probably not more than a dozen have been reported.

The neurological aspect of the disease has been carefully studied by a large number of observers, notably Goldflam,[5] Oppenheim,[6] Taylor,[7] Mitchell,[8] and Oddo and Darcourt.[9] A discussion of the etiology of the disease will be found in Singer's[10] and in Buzzard's[11] papers.

Pieces of muscle have been excised by Goldflam, Oppenheim, Crafts,[12] and Singer. All have described the microscopic appearances as "abnormal." Oppenheim found waxy degeneration. Goldflam and Crafts described the fibers as being hypertrophied and vacuolated, and Crafts also says that there is an increase in fibrous tissue. Singer found extensive fissuring in the cut sections which he considered an artifact, but which he thinks would not have been present unless there were "some essential abnormality in the muscle fibers to produce such uniform and unusual appearances."

The toxicity of the urine during an attack and interval have been studied of Goldflam, using Bouchard's method, who found that "during attacks there was a distinct increase in the urotoxic coefficient, the increase in some cases being nearly fourfold." This author found that the knee-jerk was diminished in rabbits after the injection of urine collected during an attack, but failed to get changes in the electrical reactions. Singer, using the same method, found that during an attack the urine was definitely more toxic than during an interval. Mitchell, also using this method, found no difference in the urotoxic coefficient before and during an attack. These findings are of purely historical interest.

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[1] Family Periodic Paralysis, Jour. Nerv. and Ment. Dis., 1898, xxv, 637. Continued same, p. 719.

[2] Case of Family Periodic Paralysis with Digest of Literature, Brain, 1901, xxiv, 257.

[3] Zur Frage der Periodischen Paralyse der Extremitäten, Russische Medizinische Rundshau, 1908, vi, 454.

[4] La Paralysie Périodique, Gaz. d. höp., Paris, 1911, p. 1327.

[5] See Taylor, loc. cit.

[6] See Taylor, loc. cit.

[7] Loc. cit.

[8] Case of Family Periodic Paralysis, Amer. Jour. Med. Sci., 1899, cxviii, 513.

[9] Les réactions électriques dans la paralysie familiale périodique, Archiv d'Electric. Med., 1902, xi, 1.

[10] Loc. cit.

[11] Three Cases of Family Periodic Paralysis, Lancet, London, 1901, ii, 1561.

[12] Fifth Case of Family Periodic Paralysis, Amer. Jour. Med. Sci., 1900, cxix, 651.

The toxicity of the blood serum was studied by Mitchell and by Mitchell, Flexner, and Edsall,[13] but the results were apparently negative.

Crafts has extracted from the feces during an attack a toxic substance which, when injected into rabbits and guinea-pigs, produced a transient paralysis. He does not appear to have controlled his results. Two authors, Mitchell and Mailhouse,[14] on attempting to draw blood for examination found that it clotted with great rapidity, but did not determine the coagulation time by any accurate method.

Upon the urine a large amount of work has been done. Mitchell has made analyses of total nitrogen, urea, uric acid, sulphur, and phosphates, but does not give the diet in detail, so that the significence of the results is uncertain. Crafts found an increase in ethereal sulphates during an attack, but he also fails to record the diet. The same is true of Singer's complete analyses.

Mitchell, Flexner, and Edsall[15] determined the total nitrogen of the food and urine and of ammonia and creatinin in the urine, the latter by the old Neubauer-Salkowski method (before Folin's method was published), which is undoubtedly far from accurate. The ammonia was continuously low, and the creatinin was very low for a day or two before attacks, and during the first part, and rising sharply, just after or during the latter part of the attacks.

Holtzapple[16] made a large number of urinary examinations, urea and indican being the chief things recorded. The diet is not mentioned, nor the method for determining urea. In general (average of a large number of cases), he found that the urea elimination seemed below normal and the indican increased.

Mailhouse has found a striking reduction in calcium and magnesium in spite of the fact that his patient was on a liberal diet containing more or less milk. He also found in the urine on several occasions a proteose-like body which decreased during attacks, and in addition practically always found creatin in the urine. The creatinin was somewhat higher just before the attack rather than afterward, as in Mitchell, Flexner, and Edsall's case. The methods used are not given, nor is the diet recorded in detail. Several authors have mentioned a high indican test during attacks; the same has been found to be true in our case.

Atwood[17] found in one of his cases that the intestinal flora contained a marked preponderance of the Bacillus aërogenes capsulatus.

In regard to the ordinary blood examination, moderate leukocytosis has been found by Goldflam, Taylor, and by Singer.

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[13] Physiological and Chemical Study of Three Cases of Family Periodic Paralysis, Brain, 1902, xxv, 109.

[14] Observations on a Case of Family Periodic Paralysis, Jour. Nerv. and Ment. Dis., 1910, xxxvii, 209.

[15] Loc. cit.

[16] Family Periodic Paralysis, Penn. Med. Jour., 1903, vii, 408.

[17] Family Periodic Paralysis, New York State Jour. Med., 1913, xii, 579.

The most recent papers on this disease are those of Gardner,[18] who reports a typical case, and discusses the etiology and treatment, and of Diller and Rosenbloom,[19] who studied the nitrogen, sulphur, calcium, magnesium, phosphate, and fat metabolism during an interval only.

Gardner believed the condition to be due to an intoxication, and on that hypothesis treated his patient by catharsis, low protein diet, avoidance of alcohol, together with caffein, digitalis, and bromides during an attack, and got marked improvement.

The only positive findings of Diller and Rosenbloom were a marked decrease in creatinin and an increase in undetermined nitrogen. The average creatinin coefficient was 4.8.

Case Report.—The clinical data on our case are as follows:

J. T. S., male, aged thirty-five years; weight 83.6 kilograms.

The disease has been in the family for five generations; the history is absolutely typical, namely, attacks of complete flaccid paralysis of all the skeletal muscles save those of the face, of deglutition, and of the eye muscles, lasting from six to forty-eight hours, and coming on at irregular intervals, the longest interval being seldom over six days, the sphincters and diaphragm not being involved, the reflexes and electrical reactions being diminished, or abolished during the height of the more severe attacks, and the patient being perfectly well in the intervals. Normal respiration was not involved in the paralysis, but the accessory muscles apparently were, for during the more severe attacks the patient was unable to take a deep inspiration or make a forcible expiration.

A complete genealogy showing the line of descent and the afflicted members in each generation is given in Taylor's paper.[20] Since the appearance of that paper a case has arisen in the sixth generation, a niece of the patient, aged nine years, having had several rather mild but characteristic attacks.

The patient came to the hospital at our request merely for purposes of investigation. He was in the medical wards from April 7 to May 8, 1914. During this time he had a number of attacks, some severe and some mild. The sequence and severity of the attacks are indicated in the accompanying chart. Those of April 15, April 21–22, and of May 1, were severe, there being complete paralysis of the arms, legs, trunk, and neck muscles, lasting twelve hours or more. Several other attacks, lasting a shorter period, and in which the paralysis was less complete, likewise occurred.

A complete clinical description of the attacks is also given in Taylor's paper, and since during the present stay in the hospital the attacks were entirely similar, it will be unnecessary to go into details here.

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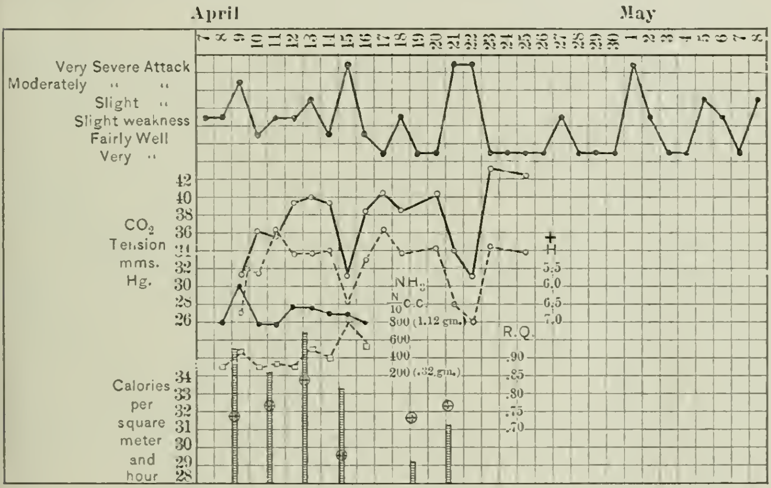
[18] Case of Periodic Paralysis, Brain, 1913, xxxv, 243.

[19] Family Periodic Paralysis, Arch. Int. Med., 1914, xiv, 869.

[20] Loc. cit.

The physical examination save for an enlarged spleen (felt two fingers' breadth below the costal margin, with increase in splenic dulness) was negative. The skeletal muscles were unusually well developed, so much so in fact that the possibility of a pseudomuscular hypertrophy was suggested. However, since the patient had a perfectly normal degree of muscular ability, being in fact rather athletic, taking much exercise, such as bicycle riding, swimming, and bowling, between attacks, this was ruled out.

Several writers have described dilatation of the heart, increase in pulse rate, and other signs of cardiac weakness during attacks. No evidence of any such occurrence was found in our case.



The upper curve indicates the patient's condition as regards paralysis from day to day. The CO_2 tension by the Plesch method is shown by solid lines and circles; by the Lindhard method, broken lines and circles. The ammonia in cubic centimeters of a N/10 solution and also in grams is shown by broken lines and squares; the hydrogen ion concentration of the urine by solid lines and dots; the respiratory quotients by circles containing crosses, and the basal metabolism in calories per square meter and hour, by perpendicular columns. The first four basal metabolism determinations are with the Benedict, the last two with the Douglas apparatus.

The urine was negative to ordinary examination save for a rather high amount of indican, which increased during attacks. This increase may not improbably be explained by the constipation which always occurred with the attacks.

. There never was any albumin except after the administration of large doses of sodium bicarbonate, and the presence of albumin, under such circumstances, cannot be considered abnormal.[21]

There were never any sugar, urobilogen, or acetone bodies.

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[21] Palmer, W. W., and Henderson, L. J., Clinical Studies on Acid Base Equilibrium, Arch. Int. Med., 1913, xii, 153.

Blood smear was negative. Wassermann test on the blood was negative.

Experimental Observations.—The findings of Goldflam, Oppenheim, and Taylor that the electrical reactions of the muscles are diminished or abolished during attacks suggest at once that the abnormality lies in the muscle itself or the end plate rather than in the nervous system. Such an abnormality might be produced by an alteration in the intermediate metabolism of the muscle cell or by some disorder of general metabolism leading to the elaboration of some circulating toxin having some special action upon muscle.

With a view to gaining information on the second alternative we have carried out the following investigations:

First of all we determined the basal metabolism. The determinations of April 9, 11, 13, and 15 were made with the Benedict respiration apparatus. The method has been described and the significance of basal metabolism discussed in a previous paper by one of us (J. H. M.).[22] The determinations of April 19 and 21 were made with a type of respiration apparatus devised by C. G. Douglas,[23] in which the expired air is collected in a rubber bag and analyzed. The gaseous exchange was determined in each of these experiments by five periods of five minutes each, on the apparatus. The figures for CO_2 and O_2 in the five periods were averaged and the calory output determined by indirect calorimetry.[24] With both types of apparatus the patient was examined in the morning during complete muscular rest, and in the *nüchtern* condition. The results of these experiments are shown in the chart. The metabolism is expressed as calories per square meter of body surface per hour. The body surface was calculated from Meeh's formula.[25]

With a view to finding out whether any acidosis occurred during the attacks, the alveolar carbon dioxide tension was determined daily from April 9 through April 23. Two methods were used: (1) Four of the so-called B samples of Lindhard were taken and the results averaged. The method has been described by Lindhard.[26] (2) A determination by the Plesch method[27] was made. The Lindhard method gives the CO_2 tension of the arterial, the Plesch of the venous blood. The Plesch determinations, therefore, are always a fewer millimeters higher than the Lindhard, but should show similar fluctuations if an acidosis is present.

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[22] Studies of Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxvii, 121.

[23] Jour. Physiol., vol. xlii; Method for Determining Respiratory Exchange, Proc. Phys. Soc., 1911, vol. xvii.

[24] Williams, Riche, and Lusk, Animal Calorimetry II, Jour. Biol. Chem., 1914, xii, 349.

[25] Body surface $= 2.3\sqrt[3]{\text{weight}^2}$ (grams).

[26] Excitability of Respiratory Centre, Jour. Physiol., 1911, xlii, 343. See also Krogh, A., Apparatus for Study of Muscular Work, Skand. Archiv. f. Physiol., 1913, xxx, 383.

[27] Hämodynamische Studien, Ztschr. f. Exper. Path. u. Therap., 1909, vi, 380.

An inspection of the results which are given in the chart will show a striking fall in both sets of samples occurring with the attacks of April 9, 15, and 21 to 22.

These drops in CO_2 tension at once suggested that an acidosis was present during attacks, so certain other tests were carried out to throw further light on the subject, but unfortunately failed to do so.

The hydrogen ion concentration of the urine was determined by the method of Henderson and Palmer.[28] In the attack of April 9 it increased from 6.5 to 5.5, but showed no rise in that o' April 15.[29]

The titratable acid in the urine was not increased during the attacks.

The urinary ammonia showed a rise in the attacks of April 15, but not in that of April 9.

The response to alkali both during intervals and attacks was normal, namely, after the ingestion of 5 grams of sodium bicarbonate, marked decrease in the hydrogen ion concentration occurred within two hours, and was accompanied by a decrease in the ammonia, apparently corresponding to that found in normal individuals.[30]

Determinations of the lactic acid in the blood and in the urine, both during an attack and in an interval, were made by Ryffel's method.[31] The results were all within normal limits. The blood varied from 10 to 21 mgm. per 100 c.c. and the urine from 11 to 16 mgm. per twenty-four hours.

An attempt to find further evidence of an acidosis was also made by determining the dissociation curve of CO_2 free blood by Barcroft's method.[32] This constitutes a test for an excess of non-volatile acids in the blood. The results were negative; specimens of blood taken both during an attack and interval gave approximately the same percentage saturation when exposed to an atmosphere of 17 mm. of oxygen tension, the figure being 62 per cent. interval, 58 per cent. in an attack; the normal limits given by Barcroft being from 65 per cent. to 75 per cent.

The total nitrogen and creatinin in the urine showed nothing abnormal. On a purin-free diet the total nitrogen in the urine was from 10 to 13 grams per day. The creatinin showed no changes during attacks as compared with the intervals. It was regularly about 1.5 grams per day. Creatin was occasionally present both during attacks and in the intervals, being from 0.1 to 0.2 grams per day.

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[28] Intensity of Urinary Acidity, Jour. Biol. Chem., 1913, xiii, 393.

[29] We are indebted to Dr. Palmer for the hydrogen ion determinations, the ammonia and titratable acidity of the urine and the lactic acid determinations on blood and urine.

[30] Henderson, L. J., and Palmer, W. W., Extreme Variation of the Concentration of Ionized Hydrogen in Human Urine, Jour. Biol. Chem., 1913, xiv, 81.

[31] Method for Lactic Acid in Urine, Jour. Physiol., vol. xxxix; Proc., p. 5.

[32] Lewis, Ryffel, Wolf, Cotton, and Barcroft, Dyspnea in Cardiac and Renal Patients, Heart, 1913, v, 45.

The blood showed a high non-protein nitrogen content. Three observations, two during an attack, one during an interval, showed the same result, 74 mgm. per 100 c.c. Uric acid and urea were retained in such proportion as would be expected with the degree of nitrogen retention. Creatinin was absent from the blood during one attack and during the interval was present within normal limits.[33]

The sulphonephenolphthalein excretion was normal during an interval, 61 per cent. in an hour and ten minutes.

Indican was nearly always present in the urine and showed a marked increase during attacks, but on a low protein diet there was but a trace, except during an attack, when it again increased.

The patient was seen again on January 9, 1915. After leaving the hospital in May, at our advice (because of high blood nitrogen), he went on a low protein (no meat) diet and remained on the same until the middle of September. During this period he was singularly free from attacks; never stayed in bed later than 11 A.M. all summer. In the fall he returned to a general diet and has continued it ever since. From October 15 to November 15 he had several rather mild attacks. Since then he has been better than ever in his life. Three-quarters of the time he has been up at 7 A.M. and never has been in bed later than noon. In the latter part of November he began to work on a steady job (outdoor salesman), a thing he has never done before.

A specimen of blood was examined for non-protein nitrogen, on this visit of January 9, 1915, and was found approximately the same as when in the hospital, 67 mg. per 100 c.c. of blood. The urine contained a moderate amount of indican, otherwise was negative.

DISCUSSION. Of the above observations, the fall in CO_2 tension is by far the most striking. Since the curves taken by two entirely different methods are in close agreement we feel that they are perfectly reliable. The possible known explanations for a fall in the CO_2 tension are the development of an acidosis and an increased sensitivity of the respiratory centre.

The latter might be produced by the stimulating action upon the centre of some circulating toxin. The methods used in searching for other evidence of an acidosis proved negative, except that in one attack there was an increase in the hydrogen ion concentration of the urine and in another, a rise in the ammonia. No evidence was found for supposing it to be a lactic acidosis. The Barcroft test showed no evidence of an increase in the non-volatile acids in the blood. The reaction to alkali being normal both during attacks and intervals is strong evidence against an acidosis in the ordinary sense. As mentioned above, there never were any acetone bodies in the urine.

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[33] We are indebted to Dr. W. Denis for the nitrogen and creatinin determinations in the urine and blood.

We therefore are strongly inclined to the hypothesis that the fall in CO_2 tension is due to an increased sensitivity of the centre, and the most likely cause for this would seem to be an intoxication of some sort.

In regard to the basal metabolism it will be noticed that the results with the Douglas apparatus are both lower than any with the Benedict apparatus. This is undoubtedly the result of a systematic error with the Douglas apparatus, due to a decreased ventilation of the lungs, since the subject breathes against a slightly increased pressure. However, the two Douglas experiments should be comparable one with another, though not with those done by the Benedict method.

The experiments (both methods) were all quite satisfactory with the exception of that of April 15, in which the different periods were not in close agreement and the R. Q. gave an impossible value, being below 0.7. The R. Q.'s in all the other experiments were between 0.78 and 0.88, which is as close as is often obtained on different days in the same individual. Disregarding then the experiment of April 15, we find that the basal metabolism determined with the Benedict apparatus on April 9 and 13 (days on which there was an attack) was higher than on April 11, when he was fairly well. Also, that in the case of the Douglas experiments, that of April 21, a severe attack, gave a higher value than that of April 19, when he was unusually well. In other words, the basal metabolism of this patient is apparently higher during attacks than in the intervals. This is rather extraordinary, for one would expect the metabolism to be lower during the enforced, and hence more complete muscular rest present while the patient is paralyzed. This increase in metabolism might reasonably be interpreted as being a further bit of evidence in favor of an intoxication.

The retained non-protein nitrogen in the blood is interesting, but we are at a loss to explain it. The urine showed no evidence of nephritis; there was no cardiac hypertrophy or hypertension, and the 'phthalein excretion was normal. It is also of interest to note that the retained nitrogen persisted after eight months, although during that time there had been marked improvement in the periodic palsy.

The creatinin in the urine showed no change during attacks, as was found in the case reported by Mitchell, Flexner, and Edsall.[34] The creatinin coefficient was 6.6, which is nearly up to the normal low limit of 7 given by Shaffer.[35] Hence the low coefficient found by Diller and Rosenbloom[36] is not a constant feature in this disease.

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[34] Loc. cit.

[35] Excretion of Creatin and Creatinin, Amer. Jour. Physiol. 1908, xxiii, 1.

[36] Loc. cit.

No definite conclusions can be drawn from these scattered observations. We think, however, enough positive findings were obtained to make it seem probable that this disease is one of metabolism and not of nervous origin. The question of acidosis is certainly worthy of further study,[37] and the hydrogen ion concentration of the blood might yield valuable information. We had not the facilities for performing this test.

Gardner's case showed a striking improvement on eliminative treatment and low protein diet. Also in our case an improvement dated from the time he began such a diet, though when he returned to a general diet the improvement continued. It is only fair to bear in mind that many observers have reported a tendency for this disease to improve with age, so it is quite possible that J. T. S.'s improvement was part of the natural sequence of events and had nothing to do with the low protein diet.

We should hardly agree with Diller and Rosenbloom, who thought that their patient's freedom from attacks while in the hospital was due to the low protein diet that he was getting. He had just had a very severe attack; in our patient's case after a very severe attack he is nearly always unusually well for a week or so. We do believe, however, that a low protein diet is worthy of a trial, and may, over a long period of time, have some influence over the number and severity of the attacks.[38]

THE ROLE OF SYPHILIS IN HYPERTENSIVE CARDIOVASCULAR DISEASE.[1]

By Henry Farnum Stoll, M.D.,

ASSISTANT PHYSICIAN TO THE HARTFORD HOSPITAL, HARTFORD, CONN.

The steadily increasing mortality from diseases of the cardiovascular system at a time when the deaths from the communicable diseases are decreasing, is a problem of great seriousness. The victims, for the most part, are not from the ranks of the aged who have run their course, but from those who have just attained that period of life when they should be of the greatest value to the family and the State.

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[37] The patient has for several years been in the habit of taking potassium citrate when he felt an attack coming on. He is not certain whether it ever did any good.

[38] At the suggestion of Dr. W. B. Cannon, the effect of adrenalin was tried in one attack; the tendency of adrenalin to lessen the fatigability of muscle being the point in mind. Adrenalin 1 to 1000 solution ♏xv, was given subcutaneously every hour for three doses. The blood-pressure was raised 12 mm., but no change at all was found in the paralysis.

The effect of physostigmin was also tried in an attack. Gr. $\frac{1}{100}$ was given every hour for four doses (subcutaneously). This also failed to have any apparent effect on the paralyzed muscles.

[1] Read before the Hartford Medical Society, April 5, 1915.

That it is a question for serious thought the recent statistics of Louis I. Dublin,[2] of the Metropolitan Life Insurance Company, clearly show.

In the ten years ending with 1910 the mortality from cerebral hemorrhage and apoplexy had increased to 18.8 per cent.; that from organic diseases of the heart, 39.3 per cent. The deaths from Bright's disease showed an increase of 18.1 per cent., and most astounding of all the mortality from disease of the arteries had risen from 5.2 to 25.8, or 396.2 per cent.

An important factor, probably the determining factor in this vascular degeneration, is the strenuous life we lead in this country, where "step lively" is the watchword. But will overwork alone account for this? A perfectly constructed motor, properly cooled and oiled, will run a long time at high speed. But an imperfection in a bearing, a piston ring that binds, or a loose connecting rod, spells disaster.

To the abuse of alcohol, the poison of lead and lues, and hard labor, most of the arterial changes are attributed. While definite knowledge, in spite of much experimental work, is very meager, it is probable that there are a considerable number of toxins, endogenous and exogenous, that exert a deleterious effect on our cardiovascular tissue.

It has been recognized for many years that syphilis shows a marked predilection for the arteries; but it was not until the advent of the Wassermann reaction and the more recent luetin test of Noguchi that it became possible to ascertain its real importance. With a few exceptions the possibility that congenital lues might be the underlying cause in some of the hypertensive cases occurring in middle life does not appear to have been considered by writers on this subject.

In the discussion of a case of congenital syphilis, reported by Messenger[3] in 1871, which showed at autopsy an interstitial nephritis, it was suggested that such a condition might prove to be the starting-point of a nephritis in later life.

Southerland and Walker[4] found at autopsy on an infant of sixteen months, whose father had had lues and died of heart disease, an endarteritis of the cerebral arteries and an interstitial nephritis. They agree with Guthrie, whom they quote, that it is probable that both congenital and acquired syphilis plays an important role in the interstitial nephritis of the adult. Hintzelman[5] shares this view. Cassel[6] found renal changes in ten out of twelve infants with congenital lues who came to necropsy.

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[2] American Journal Public Health, 1913, iii, 1272.

[3] Quoted by Armstrong, British Med. Jour., 1914, i, 958.

[4] British Med. Jour., 1903, i, 959. [5] Zeitschr. f. Kinderh., 1913, ix, No. 1.

[6] Quoted by Power and Murphy, System of Syphilis, Oxford University Press, 1908, i, 358.

In a recent paper[7] I have cited several cases with hypertension, which were apparently associated with a prenatal syphilitic infection. The material for this article comprises four groups of individuals and being so divided, attacks the problem of cardiovascular disease from somewhat different angles.

The first comprises fifty patients seen in office and consultation work, and for the most part represents individuals who experienced but slight inconvenience from this condition and were not incapacitated from their duties.

The second group is made up of one of the terminal stages of arterial disease, viz., the apoplectics. The third group, a very small one, consists of widows whose husbands had died from one of the above causes. The fourth comprises individuals, one of whose parents either has some cardiovascular-renal disorder, or had died from apoplexy, sudden cardiac failure or "kidney trouble."

Group I.—There were in all 50 cases, all white, with a systolic pressure over 160. Thirty-five (70 per cent.) were women, 15 (30 per cent.) were men. This sex distribution is almost the exact opposite of Janeway's[8] statistics. In his series of 458 cases the males were 67 per cent. Nettleship,[9] however, found that of eighty children under thirteen years of age with interstitial nephritis, 64 per cent. were females against 36 per cent. males; and this is in accord with Sawyer,[10] whose 40 cases of interstitial nephritis under thirteen years of age showed 69 per cent. females and 31 per cent. males. In parenchymatous nephritis in children Nettleship found the males slightly in excess.

None of the cases in this series suffered from lead poisoning, but two had used alcohol to excess. The cases of Group I can, with considerable exactness, be placed into one of three classes.

A. Those who either admit a primary lesion or who are known to have lived in intimate association with one who had syphilis or whose children exhibit some manifestations of hereditary lues.

B. Those individuals who, denying a venereal infection, had either a family history of cardiovascular disease (often the sudden death of parent in early life) or whose history suggested congenital syphilis, whether in the patient or in some other member of the family.

C. Patients whose history suggests neither acquired nor hereditary syphilis.

Such a classification is open to criticism because of obvious possibilities or error. Thus Case 11 had been very devoted to a dipsomaniac brother, who had acquired syphilis and who now has a strongly-positive Wassermann. Her opportunities for infection were probably many, yet she not only gives no history suggestive of primary or secondary manifestations, but her ill health very definitely antedates the time of her brother's infection. Accordingly she is classed as an acquired case, though it is quite possible that it was an hereditary one, as both of her parents died of "kidney trouble."

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[7] Stoll, Jour. Amer. Med. Assoc., 1914, lxiii, 1558.

[8] Archiv. Int. Med., 1913, xii, 755.

[9] Trans. Ophth. Soc., iii, 51. Quoted by Sawyer, vide No. 16.

[10] St. Thomas' Hospital Reports, 1906, xxxv, 459.

In like manner Case 41, placed in Class C, might be with some reason grouped with those probably exposed to syphilis, as her husband died from pernicious anemia. Acknowledging these limitations, this division, nevertheless, has much that is suggestive.

Taken as a whole the Wassermann test was made on 42 of the cases in this group, with $33\frac{1}{3}$ per cent. reacting positively. The luetin test was used in 45 cases, 82 per cent. of whom were positive. In subdivision A of Group I are 17 individuals for the most part with a good family history, who either admit having had syphilis or were presumably exposed to infection in the family, or who have children exhibiting some signs of a congenital infection.

The Wassermann was positive in 61.5 per cent. of these cases and the luetin test in 76 per cent.

It is subdivision B of this group which consists of individuals from families prone to cardiovascular disease that I desire especially to draw your attention. There are 19 patients in this class and the Wassermann was positive in only 12 per cent., while the luetin test was positive in 89 per cent.

Neither the Wassermann nor the luetin test was positive in 17 cases, or 89 per cent., and one who reacted negatively to both tests (Case 28) is undoubtedly of specific origin, as will be evident when the history is reviewed in detail.

C. In the fourteen cases whose personal history does not suggest an acquired infection and whose family history is not that of cardiovascular disease the Wassermann was positive in $33\frac{1}{3}$ per cent., and the luetin in 82 per cent. It is quite likely that these were chiefly acquired cases notwithstanding the negative history.

For years neurologists have recognized that syphilitic infection in certain families tends to be manifest by various disorders of the nervous system; thus a husband may be tabetic, the wife paretic, and certain children exhibit paresis or possibly cerebral syphilis. In one family mentioned by Nonne[11] paresis was present in three generations. There is much from the clinical stand-point to suggest a strain of spirochetes with special affinity for nervous tissue, and Nichols[12] has isolated a strain which appears to have this property. A study of the cases here presented suggests there is a type of familial cardiovascular syphilis. While the occurrence of these lesions in parent and child might be explained by the inheritance of poor vascular tissue, this would not explain the occurrence in both husband and wife of cardiovascular syphilis. It remains to be seen if there exists a strain of spirochete with special affinity for vascular tissue.

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[11] Syphilis and the Nervous System (English translation), 1913.

[12] Jour. Amer. Med. Assoc., 1914, lxiii, 466.

An instance of familial cardiovascular degeneration, of which syphilis appears to be the cause, is the following:

The grandparents died from cardiac disease, an uncle in early life of apoplexy, and an aunt suddenly from heart disease. One living aunt had had several strokes of apoplexy, and her unmarried sister gives a positive luetin test, though a negative Wassermann. Two of the third generation are unmarried—middle-aged women with hypertension. One gave a positive luetin with a negative Wassermann. In the other both tests were negative, but as a girl she had a persistent ulceration of the rectum which was followed by a stricture that required removal. One brother who knows of no infection gave a positive luetin test, another is stated to have a chronic ulcer near his anus and to "shed the soles of his feet" periodically. A third brother died suddenly of heart disease when sixteen years old. In view of the family and personal history the sister with hypertension in whom both the Wassermann and the luetin tests were negative is classed as luetic. The mother of this generation died suddenly of cardiac dilatation following pneumonia, and the presumption seems warranted that she probably had a syphilitic myocarditis.

What we might term "the syphilitic lead" in the history of Case 21 is not so much that both parents and a sister died from nephritis, as the fact that the patient and two of her sisters all became deaf in early womanhood without apparent cause. Insidious deafness is a common result of congenital lues. It is noteworthy that the highest pressure (270 to 280 auscultatory, wide cuff) was in a woman with an hereditary infection. Only once have I met with a higher pressure, and that was in an unmarried woman, aged forty-nine years, whose mother, aged sixty-nine years, had died of a "shock," though she had her first stroke several years before. In this woman the systolic pressure was 300, diastolic 160, and there was an accompanying aortitis and nephritis. It seems quite possible that this was an inherited syphilis also. The further history of this case is of interest. She developed a tonsillar diphtheria one week after I saw her, and though she had antitoxin promptly, she died in about a week from cardiac failure; the pressure steadily fell until the end.

Several of these cases would not have been detected except for my custom of examining, whenever possible, the parents of patients suspected of having hereditary syphilis. In one instance the mother of a young man with interstitial keratitis was found to have a blood-pressure of over 160.

In another case the father of an anemic child with a positive Wassermann and of two children who were deaf and dumb was found to have hypertension and a strong luetin reaction. In a third instance the mother of a girl who had precordial pain, had an aortitis and systolic blood-pressure of 194. The mother's sister also had aortic disease with a systolic pressure of 220.

Case 31 is of interest, as mercury and salvarsan are theoretically contra-indicated with marked kidney involvement. Notwithsatanding that the patient had diabetes and eliminated only a trace of 'phthalein in two hours, she experienced much symptomatic relief from three injections of neosalvarsan and a course of mercury injections combined with the iodide of potassium. She was first given mercury by mouth, then by injection, and as no untoward effects were noted, neosalvarsan was finally administered. The amount of 'phthalein eliminated a year later was over 15 per cent. The blood-pressure was lower and the patient felt much better. The Wassermann is still very positive, though the general condition is good, except for glycosuria.[13]

A woman, aged forty-two years, consulted me because of increasing weakness and a thoracic pain which she feared might be due to pulmonary disease. There was nothing to be found in her lungs, but her systolic pressure was 170, diastolic 115. The Wassermann reaction, even with fortified antigens was negative. Upon questioning her husband I learned that he had an initial lesion twenty-two years previously, for which he had received practically no treatment. He was married sixteen years ago and four years later he had a recurrence of mucus patches and sore throat which subsided after a few weeks' medication.

He considers himself in perfect health, but his Wassermann is strongly positive and both he and his wife gave a marked luetin reaction.

Of especial interest in this case is the fact that an innocent infection may take place years after the chancre from recurring mouth lesions. It also demonstrates that apparent health is compatible with an active syphilitic infection as revealed by the Wassermann test.

The accompanying illustration shows the wife's luetin reaction, and is typical of the average reaction obtained in this series. In three or four cases, however, the resulting pustule was very much larger than the one shown here.

While it is true that a high percentage of hypertensive cases are suffering from interstitial nephritis, Gull and Sutton asserted years ago that similar changes could be found in the smaller arteries throughout the body, though they were usually most marked and easiest of demonstration on the kidney. This conception of hypertensive disease, as a condition affecting the smaller arterioles throughout the body, is the one generally accepted today.

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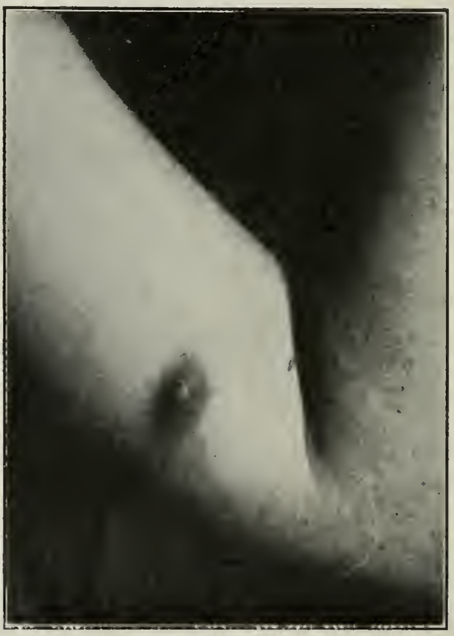
[13] The day proof was corrected she died after being comatose three days. Excellent health up to first convulsion. *Urine* loaded with sugar.

In some of these cases the examination of the urine suggested a small granular kidney; in the majority it was negative. Several were given the 'phthalein kidney function test and the results are recorded in a separate column. For the most part good function is shown.

Group II.—The cases of apoplexy, fifteen in all, were nearly all patients in the Hartford Hospital, and in only a few could any history be obtained, owing to their mental condition. Six were under sixty and nine were older. The oldest was a hale old man of ninety-one, who made an excellent recovery from a slight shock.



Positive luetin reaction in woman with hypertension whose Wassermann was negative. In addition to the pustule there is a well-marked areola. Both the Wassermann and luetin tests were positive in the husband.

He had an initial lesion nearly fifty years before, though he remembered no secondaries. His leutin test was definitely positive. Of the group under sixty, 20 per cent. gave a positive Wassermann reaction and 83 per cent. a positive luetin. Only one of the older group had a Wassermann, and it was negative. The luetin was positive in 55 per cent. of those over sixty. This group is so small that one would be unwarranted in concluding that the same percentage would obtain in a large series. It demonstrates, however, that syphilis is a very common factor in apoplexy, irrespective of age.

The spinal fluid was examined in five cases of apoplexy. In several there was a slight cellular increase and a positive globulin test with a negative Wassermann reaction and a positive luetin. The Wassermann in blood and spinal fluid agreed in all cases. In most instances only 0.2 c.c. of fluid was used; with larger amounts the percentage of positive Wassermann's would probably have been somewhat higher. Two cases were of specially interest as showing the difference between an acquired infection and one that was presumably congenital. A man, aged fifty years, with a right hemiplegia, was referred to me by Dr. E. A. Wells. He had had a chancre some years before. The Wassermann in both blood and spinal fluid was very positive, and in the latter there was a marked globulin increase; cells not counted. The other, a man aged thirty-six years, with a left hemiplegia, was seen with Dr. Cantarow. He denied absolutely any venereal infection and the arch of his palate was exceedingly high and narrow, which is almost pathognomonic of hereditary lues. The blood and spinal fluid Wassermann reaction was negative, though 1 c.c. of fluid was used. There was no cellular increase and no globulin. Both patients exhibited a strong luetin test.

Group III.—It was my privilege to test seven widows whose husbands died from cardiovascular or renal disease in middle life. The Wassermann was done in six, and was positive in half (50 per cent.); the luetin test was positive in all (100 per cent.), though in one in whom the Wassermann was very strong it did no develop until the sixth week.

Group IV.—Group IV is made up of thirty-seven individuals, children and adults who knew of no venereal infection, and who either gave a history of parental death from heart disease, apoplexy, or "kidney trouble" (usually in early life), or had a parent living with one of the above maladies. The latter were few. Twelve of this group were included in the Class B of Group I. Thirty-four, or 89 per cent., gave either a positive Wassermann or luetin reaction. Many appeared to be in good health, but the majority had some complaint, and in a number of instances symptomatic improvement followed syphilitic treatment. I do not consider this percentage as fairly estimating the amount of hereditary lues in cardiovascular families. As nearly a third of the cases were patients who came for examination because of some evidence of ill health, this percentage would have undoubtedly been lowered considerably if the number of apparently healthy individuals studied had been greater. In a previous study of syphilitic families irrespective of health, I found 59 per cent. to be infected, and of those who appeared to be perfectly healthy, the luetin test was positive in 39 per cent.

Furthermore, it by no means follows that the various symptoms complained of by this group were in each instance due to lues, solely because the Wassermann or luetin test was positive. The patient with aortitis may have gall-stones, or the stomach symptoms may be due to cancer, even though lues is admitted. Nor are we justified in assuming that in all of this group the infection was hereditary because no history of infection could be obtained. Granting these limitations, the fact remains that a large percentage of the offspring of cardiovascular parents have a prenatal infection. (See Case 10.)

It is probably true, and indeed most fortunate, that syphilitic infection does not always mean clinically syphilitic disease. By this I mean that an infection may be more or less dormant for years and finally die out without in any way appreciably affecting the health of its host or shortening his life. But while admitting this possibility, we have as yet no means of ascertaining in which case this will happen and in which disaster will follow.

Most of the Wassermann tests in this series were made by Mr. R. V. Story at the laboratory of the State Board of Health, which is under the direction of Prof. Conn, of Wesleyan. A number were done by Dr. Jessie Fisher at the State Hospital at Middletown, one in the laboratory of Dr. J. A. Fordyce, of New York, and several by Drs. Russ and Brayton, of this city. The luetin was very kindly supplied by Dr. Noguchi, of the Rockefeller Institute.

Cholesterinized antigens were employed in thirteen cases, and their more general use would have given a somewhat higher percentage of positive results. Nevertheless, several negative results were reported from each of the four laboratories in late congenital cases when the luetin test was positive; this was obtained several times even when fortified antigens were used. Provocative injections of salvarsan would undoubtedly have increased the number of cases exhibiting a positive Wassermann, but even if the reaction remains negative, lues cannot be absolutely excluded. The luetin reactions were for the most part of unusual severity, probably due to the fact that the patients were, as a rule, given a small amount of potassium iodide for a time previously. This seems to "activate" the test even better than mercury or salvarsan.

The luetin test has been used about 10,000 times, Dr. Noguchi tells me, by over 100 different observers, and with but very few exceptions all agree that the test is specific for lues; as specific in fact as the tuberculin test for tuberculosis.

Kaliski,[14] testing Hebrews at the Montefoire Home, questioned the specificity of the papular type of reaction. It seemed incredible to him that so many orthodox Hebrews could have a latent syphilitic infection, especially in the absence of the more common signs of syphilitic disease.

As a matter of fact, syphilitic disease, especially of the aorta, is very common in this race. That in many cases the luetin test may be an indication of an hereditary infection is a possibility that has so far received insufficient consideration.

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[14] New York Med. Jour., 1913, xcviii, 24.

In a few instances where "activation" with mercury and potassium iodide was omitted before giving the test the reaction was papular in type and of moderate severity, while the Wassermann was very positive. Emory,[15] Wilson,[16] and others have drawn attention to the fact that in the late manifestations of hereditary syphilis the luetin test is more often positive than the Wassermann.

Vedder and Borden,[17] comparing the Wassermann and the luetin test in a series of over 700 individuals in whom they employed cholesterinized antigens, say "it is apparent that in tertiary latent and treated cases the luetin test is apparently more efficient in detecting syphilis than the most efficient Wassermann." Eighty per cent. of the patients tested by Borden and Vedder were between fifty and eighty years of age, and suffered from the various degenerative processes that attend that period of life. The combined results of the Wassermann and the luetin test revealed the fact that over 45 per cent. had been infected with syphilis.

Valuable as the Wassermann and the luetin tests are in the diagnosis of obscure cases, it is very unfortunate when they are used as short cuts to diagnosis, as neither test is infallible. It takes less time to obtain blood for the Wassermann reaction than it does to go over the family and personal history with a fine tooth comb, as it were. A carefully obtained history may be supplemented but not supplanted by either the Wassermann or luetin test.

Treatment.—In addition to the usual regime adopted in these cases it was possible to observe the effect of specific treatment on several patients. The number is altogether too small, however, to draw any conclusions as to the relative value of the different forms of antiluetic treatment. Mention has been made of the great improvement in a patient with aortitis and diabetes who was excreting only a trace of 'phthalein in two hours.

I am far from being sure that salvarsan is indicated in all cases. Sometimes an important military position can be taken by a long siege where an assault would fail. Several patients have exhibited very satisfactory improvements in subjective symptoms, usually coincident with some lowering of the blood-pressure following several months of mercury injections combined with potassium iodide by mouth. Inunctions give satisfactory results, but their field of usefulness is limited in private cases.

Mercury by mouth has not seemed to be so efficacious. The urine of these patients has been carefully watched and rarely has there been signs of kidney irritation. In four instances the kidney function was determined before treatment was instituted and several months later. The results are shown in the following table.

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[15] Lancet, 1914, i, 223.

[16] Quoted by Armstrong, vide note 2.

[17] Vedder and Borden, Jour. Amer. Med. Assoc., 1914, lxiii, 1750.

TABLE SHOWING PHENOLSULPHONEPHTHALEIN ELIMINATION.

	Before treatment.				After treatment.				
Case No.	Date.	Per cent. 1st hour.	Per cent. 2d hour.	Total per cent.	Date.	Per cent. 1st hour.	Per cent. 2d hour.	Total per cent.	Medication used.
23	June 4, 1913	22	7	29	Feb. 3, 1915	47	22	70	Hg. injections; KI.
25	July 1, 1914	29	20	49	Feb. 21, 1915	56	20	76	Hg.; neosalvarsan and salvarsan.
47	May 5, 1914	39	10	49	Feb. 4, 1915	32	25	57	Hg. injections; KI.
39	Jan. 21, 1914	Trace	Trace	Trace	About June 15, 1914	Trace	Trace	less than 10	Hg. mouth; Hg. injection; neosalvarsan; KI.
					Feb. 22, 1915	Trace	15	15	

Two cases might be cited as illustrating the possibilities and limitations of specific therapy:

A married woman, aged sixty-five years (Case 23), was referred to me by Dr. Frederick Crossfield because of dyspnea. There was marked pulsation in the carotids, and the systolic pressure was 190 and diastolic 85. Rest in bed and purgation enabled her to lie comfortably with head low, but when she began to get about again in two weeks the pressure rose to over 160. For the next three months she was given injections of mercury, at first the biniodide, grain $\frac{1}{6}$, twice a week, and later the salicylate, grain $\frac{1}{10}$ weekly, together with KI by mouth. Her improvement has been most gratifying. Last summer, after a morning of "canning," her pressure was 140 and once since then was 130, though it averages about 160. Three Wassermanns were negative, but the luetin test was very strong. The increase in the 'phthalein output after several months' treatment is shown in the preceding table.

In contradistinction to this is the young woman whose systolic pressure was 270. When she had as much improvement as could be expected from the usual dietetic-rest-hot bath regime, she was given three injections of neosalvarsan and a number of mercury, though the family was told it was questionable if any improvement would follow. In the months succeeding the treatment she seemed to have a little more endurance and was much brighter. Her speech, which had been thick, improved considerably. A cough that had persisted for many months, accompanied by purulent sputum in which tubercle bacilli were never found, completely disappeared. The systolic blood-pressure remained, however, at about 270, and I cannot feel that the treatment was of any great benefit. In view of the extensive structural changes that attend such high pressure it does not seem reasonable to expect any treatment to avail. Had it been possible to have detected her syphilitic infection in her childhood as it would be today, and had she received a thorough course of treatment through a period of several years, this tragedy of middle life might have been avoided. By promptly stamping on the fuse a calamity may be averted. After the explosion there are only tears and regrets.

The results of this investigation can be summarized as follows:

1. Syphilis is the underlying or basic factor in a much higher percentage of hypertensive cases than has hitherto been realized. Of 50 individuals studied 90 per cent. either gave a positive Wassermann or luetin test, or were known to have had lues, or had children with hereditary syphilis.

2. Nineteen were from cardiovascular families. In seventeen of them either one or both test were positive. One of the two with negative reactions is surely specific. This strongly suggests the existence of what might be termed "familial cardiovascular syphilis."

3. It would seem that hypertensive disease is one of the most common—possibly the most frequent—of the so-called "late" manifestations of hereditary syphilis.

4. Apoplexy and sudden cardiac death occurring in middle life are almost always due to syphilis, and it cannot be considered a negligible factor even in the aged.

5. The remaining parent and the children of individuals dying a cardiovascular-renal death in middle life should be tested for syphilis as they are infected in a high percentage of cases.

6. Specific treatment has given very satisfactory results in a few cases for the most part individuals whose systolic pressure was under 200. The careful administration of mercury over a period of several months has not appeared to be injurious to the kidney even when there was considerable reduction of 'phthalein output. In a few instances the kidney function was increased several months after treatment.

7. The luetin test, especially if activated by a week of mixed treatment, is often of more value than the most sensitive Wassermann in detecting these late manifestations of syphilitic infection.

TABLE I.—CASES WITH AN ACQUIRED INFECTION (CLASS A).

CASE 1.—Male, aged fifty-nine years. *Diagnosis*—hypertension; systolic, blood-pressure, 195; diastolic blood-pressure, 85. *Personal History*—had syphilis years ago; perforation of nasal septum. *Wassermann:* + +.[18] *Luetin*—not done.

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[18] Wassermann reactions showing 50 per cent. inhibition are reported +. Those exhibiting more complete inhibition (75 per cent.) and the completely positive reaction, + +. The use of cholesterinized antigens indicated by *. The luetin test + signifies a papular reaction; + + pustular; the very strong reaction, + + +.

Case 2.—Male, aged fifty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 200. *Family History*—wife had several miscarriages; one child with hare-lip and imperforate anus. Family history good. *Personal History*—denies lues; alcoholic. *Wassermann:* +.* *Luetin:* +− and again + −.

Case 3.—Female, aged fifty years. *Diagnosis*—hypertension; systolic blood-pressure, 184; diastolic blood-pressure, 120. *Family History*—husband, general pains; son, hypertension and high, narrow palate with luetin, +. Daughter very narrow palate with Wassermann strongly positive. *Wassermann:* −.* *Luetin:* −.

Case 4.—Female, aged forty years. *Diagnosis*—hypertension; systolic blood-pressure, 195; diastolic blood-pressure, 110. *Family History*—husband has positive Wassermann. *Wassermann:* ++.* *Luetin*—not done.

Case 5.—Female, aged sixty-two years. *Diagnosis*—aortitis; syphilis of liver (autopsy); systolic blood-pressure, 180. *Family History*—negative. *Personal History*—husband had "soft chancres" a short time before marriage. *Wassermann*—not done. *Luetin:* + + +. *Kidney Function*—first hour 22, second hour 11, total 33 per cent.

Case 6.—Male, aged forty-seven years. *Diagnosis*—aortitis, paresis; systolic blood-pressure, 190; diastolic blood-pressure, 120. *Personal History*—chancre twenty-five years ago. *Wassermann:* + +. *Luetin:* −.

Case 7.—Male, aged thirty-eight years. *Diagnosis*—hypertension; systolic blood-pressure, 170. *Personal History*—eleven years ago had gonorrhea; no chancre; "rash" several weeks later. *Wassermann:* ++. *Luetin:* +++. *Kidney Function*—first hour 55, second hour 25, total 70 per cent.

Case 8.—Female, aged fifty-eight years. *Diagnosis*—aortitis; systolic blood-pressure, 170; diastolic blood-pressure, 80. *Personal History*—husband dropped dead, aged twenty-seven years. *Wassermann:* −. *Luetin:* ++. *Kidney Function*—first hour 60, second hour 25, total 85 per cent.

Case 9.—Female, aged forty-nine years. *Diagnosis*—aortitis; systolic blood-pressure, 190; diastolic blood-pressure, 85. *Personal History*—husband had some "disease" when married, and at once had wife start to take some medicine. *Wassermann:* −. *Luetin:* +++.

Case 10.—Female, aged thirty-eight years. *Diagnosis*—hypertension; systolic blood-pressure, 165; diastolic blood-pressure, 100. *Personal History*—husband died of "shock," aged thirty-five years. *Wassermann:* + +. *Luetin*—at first negative; at end of six weeks +. A son and daughter have positive Wassermann; a second daughter, a positive luetin test.

Case 11.—Female, aged forty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 180; diastolic blood-pressure, 110.

Family History—father and mother died of nephritis. *Personal History*—a brother had a chancre several years ago. He is very alcoholic, and sister has been very devoted to him. The brother has a Wassermann reaction positive at present. *Wassermann:* ++. *Luetin:* +++.

Case 12.—Female, aged fifty-two years. *Diagnosis*—hypertension; systolic blood-pressure, 210; diastolic blood-pressure, 110. *Personal History*—husband had syphilis. Son has a syphilitic arthritis with luetin, +. Daughter, Wassermann, ++. *Wassermann:* +−.* *Luetin:* ++.

Case 13.—Female, aged forty-two years. *Diagnosis*—hypertension; systolic blood-pressure, 170; diastolic blood-pressure, 115. *Personal History*—husband had syphilis before married and a positive Wassermann now. Sore throat recurred afterward. Only pregnancy a miscarriage. *Wassermann:* −. *Luetin:* ++. *Kidney function*—first hour 40, second hour 10, total 50 per cent.

Case 14.—Male, aged fifty-two years. *Diagnosis*—diabetes; systolic blood-pressure, 170; diastolic blood-pressure, 110. *Personal History*—son and daughter deaf and dumb, another daughter anemic with positive Wassermann. Sexually promiscuous. *Wassermann*—not done. *Luetin:* ++.

Case 15.—Female, aged fifty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 195; diastolic blood-pressure, 140. *Personal History*—son had angina (mild) with Wassermann, −. Luetin, +, cured by "606" and Hg.; daughter has severe headaches. *Wassermann:* −.* *Luetin:* +++.

Case 16.—Female, aged fifty-seven years. *Diagnosis*—aortitis; interstitial nephritis; systolic blood-pressure, 200. *Personal History*—daughter had optic neuritis; heart block; relief followed specific treatment. Wassermann. Luetin, ++. Son had headache. Wassermann, negative; luetin, +. *Wassermann*—not done. *Luetin*—not done.

Case 17.—Female. *Diagnosis*—hypertension; systolic blood-pressure, 170+. Dactylitis with necrosis. *Family History*—one stillbirth, two miscarriages, several children died young. Daughter had severe headache with Wassermann −, and Luetin +.

Table II.—CASES PRESUMABLY OF HEREDITARY TYPE (CLASS B).

Case 18.—Female, aged thirty-eight years. *Diagnosis*—aortitis; systolic blood-pressure, 180. *Family History*—two brothers died from heart disease, aged forty-five and fifty years. *Personal History*—husband knows of no venereal infection. *Wassermann*—not done. *Luetin:* ++.

Case 19.—Male, aged fifty-three years. *Diagnosis*—aortitis; systolic blood-pressure, 210; diastolic blood-pressure, 110. *Family History*—father dropped dead, aged forty-six; a twin brother dropped dead, aged forty-eight; a sister living has "heart trouble;" mother died, aged seventy-six, of arterial sclerosis. *Personal History*—knows of no venereal infection. *Wassermann*—after 0.45 neosalvarsan, –. *Luetin:* +++.

Case 20.—Male, aged fifty-eight years. *Diagnosis*—aortitis; systolic blood-pressure, 242; diastolic blood-pressure, 142. *Family History*—father died, aged forty-eight, of erysipelas. Sister[1] died from an obscure abdominal lesion. Sister[2] died from a "cerebral lesion?" Sister[3] died with mental symptoms, and for years had arthritis deformans. Brother[1] lived one day. Brother[2] has had "muscular rheumatism" for years; no lues but a positive luetin test. *Personal History*—no venereal infection. *Wassermann*—after neosalvarsan, –. *Luetin:* +++. *Kidney Function*—first hour 15, second hour 15, total 30 per cent.

Case 21.—Female, aged forty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 162; diastolic blood-pressure, 106. *Family History*—father and mother died from nephritis, also one sister. A brother and sister have hypertension. Another sister has a positive luetin test. All three sisters became deaf in early womanhood. *Wassermann:* +. *Luetin:* ++. *Kidney Function*—first hour 60, second trace, total 60 per cent.

Case 22.—Male, aged fifty-seven years. *Diagnosis*—hypertension; systolic blood-pressure, 180; diastolic blood-pressure, 110. *Family History*—father died from "shock," aged sixty-eight. Mother died at forty-five, cause? *Personal History*—no venereal infection. *Wassermann:* –. *Luetin:* +++.

Case 23.—Female, aged sixty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 190. *Family History*—father died young; cause? very alcoholic; mother died young. *Personal History*—always neurotic; first pregnancy a miscarriage. Husband has had no venereal disease. *Wassermann:* –. *Luetin:* +++. *Kidney Function*—first hour 22, second hour 7, total 29 per cent. See Table.

Case 24.—Male, aged forty-eight years. *Diagnosis*—hypertension; systolic blood-pressure, 220. *Family History*—mother died at sixty-four, of kidney disease. *Personal History*—no venereal infection. *Wassermann:* –. *Luetin:* ++. *Kidney Function*—first hour 26, second hour 13, total 39 per cent.

Case 25.—Female, aged forty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 220; diastolic blood-pressure, 120. *Family History*—mother died at thirty-two, of heart disease. *Personal History*—for several years has had joint pains. *Wassermann*—two laboratories. *Luetin:* ++. *Kidney Function*—first hour 29, second hour 20, total 49 per cent.

Case 26.—Male, aged forty-eight years. *Diagnosis*—aortitis; systolic blood-pressure, 208; diastolic blood-pressure, 120. *Family History*—father very alcoholic; mother died at forty-eight, cause?

Personal History—knows of no venereal infection; slight shock one year ago. *Wassermann*—not done. *Luetin:* +.

Case 27.—Female, aged forty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 280; diastolic blood-pressure, 140. *Family History*—marked family history of cardio-arterial disease. See text. *Wassermann:* –. *Luetin:* ++. *Kidney Function*—first hour 27, second hour 17, total 44 per cent.

Case 28.—Female, aged forty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 170. *Family History*—sister of No. 27. *Personal History*—persistent rectal ulceration as a girl. *Wassermann:* –. *Luetin:* –. *Kidney Function*—total for two hours 55 per cent.

Case 29.—Female, aged fifty-three years. *Diagnosis*—aortitis; systolic blood-pressure, 194; diastolic blood-pressure, 110. *Family History*—sister has aortitis; husband died of heart disease; daughter has angina and a very positive Wassermann. *Wassermann:* –.* *Luetin:* ++.

Case 30.—Female, aged forty years. *Diagnosis*—aortitis; systolic blood-pressure, 220; diastolic blood-pressure, 110. *Family History*—sister of preceding. *Wassermann:* +–.* *Luetin:* ++.

Case 31.—Female, aged sixty years. *Diagnosis*—hypertension; systolic blood-pressure, 180 to 220. *Family History*—father died at fifty, of heart disease; brother of Bright's disease at sixty-eight; brother of shock at sixty-eight. *Wassermann:* –.* *Luetin:* ++.

Case 32.—Female, aged forty-four years. *Diagnosis*—hypertension; systolic blood-pressure, 162; diastolic blood-pressure, 110. *Family History*—father died at sixty-four with Bright's disease of many years' duration; sister died of Bright's disease, aged fifty-three. *Personal History*—never strong; "growing pains" severe in childhood; "chronic fatigue." *Wassermann:* ++.* *Luetin:* ++.

Case 33.—Female, aged forty-six years. *Diagnosis*—arthritis of knee; hypertension; systolic blood-pressure, 160; diastolic blood-pressure, 80. *Family History*—for as many years as she can remember her mother had leg ulcers; all the children's teeth were "soft" and very poor. *Personal History*—the arthritis was markedly improved by specific treatment. *Wassermann:* – *Luetin:* ++.

Case 34.—Female, aged fifty-four years. *Diagnosis*—hypertension; hypertrophic arthritis; systolic blood-pressure, 190. *Family History*—father had a stroke at about fifty-five; mother had heart disease for years; died at seventy. A daughter has had very severe headaches for years. *Personal History*—had some psychosis several years ago. *Wassermann:* –.* Luetin –.

Case 35.—Female, aged forty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 200+. *Family History*—mother living; heart and kidney disease for many years. *Personal History*—severe growing pains when girl. Skin over patellæ very "horny" for years. *Wassermann:* –.* Luetin ++.

CASE 36.—Male, aged forty-eight years. *Diagnosis*—aortitis; hypertension; systolic blood-pressure, 230; diastolic blood-pressure, 135. *Family History*—mother died of shock at eighty; brother died suddenly at thirty-five years; had had severe headaches for years; sister has albuminuric retinitis; another sister very severe headaches. *Personal History*—denies lues; hemiplegia five months before. *Wassermann:* negative. *Luetin:* ++.

TABLE III.—UNCLASSIFIED CASES WHO GIVE NO HISTORY SUGGESTING ACQUIRED INFECTION AND WHO HAVE GOOD FAMILY HISTORIES (CLASS C).

CASE 37.—Female, aged sixty-three years. *Diagnosis*—arterial sclerosis, aortitis and mitral stenosis; systolic blood-pressure, 169 (autopsy). *Family History*—husband died at fifty-six of "Bright's disease." *Wassermann*—after neosalvarsan, —. *Luetin*: +++.

CASE 38.—Female, aged sixty-seven years. *Diagnosis*—hypertension of over ten years' duration. Systolic blood-pressure, 200. *Family History*—negative. *Wassermann:* —. *Luetin:* —. *Kidney Function*—in 2 hours over 60 per cent.

CASE 39.—Female, aged fifty years. *Diagnosis*—aortitis; diabetes; nephritis. Systolic blood-pressure, 165; diastolic blood-pressure, 115. *Family History*—husband died at sixty-two of heart disease. *Wassermann:* ++. *Luetin:* ++. *Kidney Function*—first hour trace, second hour trace. See Table.

CASE 40.—Female, aged seventy years. *Diagnosis*—hypertension; arthritis. Systolic blood-pressure, 210. *Family History*—husband has angina; denies lues. Daughter "weakling," with Luetin, +. *Personal History*—has had several slight shocks. *Wassermann*—not done. *Luetin:* +. Probably belongs in Class A.

CASE 41.—Female, aged fifty-four years. *Diagnosis*—chororetinitis; systolic blood-pressure, 200+. *Family History*—husband died at age of fifty-seven of pernicious anemia. *Personal History*—twenty years ago lost sight of right eye; three months ago left eye began to fail. *Wassermann:* —. *Luetin:* ++.

CASE 42.—Male, aged forty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 160+. *Family History*—daughter has intermittent claudication. *Personal History*—denies lues. *Wassermann:* —. *Luetin:* ++.

CASE 43.—Male, aged fifty-one years. *Diagnosis*—nephritis; paroxysmal hemoglobinuria; systolic blood-pressure, 170+. *Family History*—daughter of poor mental development; very nervous; high palate. Strong luetin reaction. *Personal History*—denies lues. *Wassermann:* —*. *Luetin:* +.

CASE 44.—Female, aged fifty-three years. *Diagnosis*—aortitis; systolic blood-pressure, 170; diastolic blood-pressure, 70. *Wasser-*

mann: ++.* *Luetin:* −. *Kidney Function*—first hour 50, second hour 18, total 68 per cent.

Case 45.—Female, aged sixty years. *Diagnosis*—carcinoma of liver and gall-stones. Systolic blood-pressure, 172; diastolic blood-pressure, 90. *Family History*—negative. *Wassermann:* −. *Luetin:* −.

Case 46.—Male, aged fifty-eight years. *Diagnosis*—detached retina; hypertension; systolic blood-pressure, 185. *Family History*—brother at thirty-eight had slight "stroke." He had no known venereal lesion. *Personal History*—no venereal infection. *Wassermann:* −. *Luetin:* ++.

Case 47.—Female, aged sixty-one years. *Diagnosis*—aortitis; systolic blood-pressure, 190; diastolic blood-pressure, 85. *Family History*—husband has angina, though he denies lues. *Wassermann*—later. *Luetin:* ++. *Kidney Function*—first hour 39, second hour 10, total 49 per cent.

Case 48.—Male, age about fifty years. *Diagnosis*—aortitis; systolic blood-pressure, 200; diastolic blood-pressure, 100. *Personal History*—denies infection. *Wassermann:* ++. *Luetin*—not done.

Case 49.—Female, aged forty-eight years. *Diagnosis*—hypertension; systolic blood-pressure, 184; diastolic blood-pressure, 84. *Personal History*—husband a drunkard; suicide. *Wassermann:* +.* *Luetin:* +.

Case 50.—Female, aged sixty-four years. *Diagnosis*—hypertension; systolic blood-pressure, 200+. *Family History*—hypertension for ten years; negative. *Personal History*—negative *Wassermann*—not done. *Luetin:* ++.

LATENT SYPHILITIC INFECTION OF THE LUNGS.

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and

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PHILADELPHIA.

The only type of pulmonary syphilis about which there is a general agreement is that seen in newborn syphilitic children. In this form of the disease, gummata may occur, but, as a rule, they are rare. The typical lesion is that known as white pneumonia. The lung presents on section a dry, smooth surface, grayish or yellowish white in color, resembling closely the cut surface of the pancreas. The process may occur in scattered patches throughout both lungs or may involve the entire lobe. This type of pulmonary syphilis is, for the most part, of pathological interest only.

In acquired syphilis most writers describe two main types of the disease as it occurs in the lungs, namely, the formation of gummata or an extensive cellular infiltration which leads to fibroid changes. If the disease assumes the indurative type, and this is by far the most common form, it usually originates at the hilus of the lung and extends outward along the bronchi and bloodvessels. The process is usually unilateral, and at most involves only a portion of one lobe; if several lobes are implicated it is the portions which adjoin the root of the lung.

In addition to these types a focal form has been described in which the lesion consists of an area of consolidation and catarrh. It is usually situated around the root of the lung, but may occur at one apex.

Whether the disease manifests itself in the form of gummata as a diffuse fibrosis or as a focal lesion, most of the cases reported indicate that the base of the lung or the area about the hilus, rather than the apex, is the part most frequently attacked. This fact is usually cited as one of the strong differential points between syphilis and tuberculosis. The general opinion has been that the apices are rarely involved, but it would be rather surprising, in view of the wonderfully diverse forms in which the localization of syphilis manifests itself, if the upper portions of the lungs should always escape.

We believe that pulmonary syphilis of a latent type occurs far more frequently than is usually supposed. The form to which we wish to call attention is that in which the localization occurs in the apices of the lungs. This type of the disease may simulate early pulmonary tuberculosis so closely as to deceive us entirely. How closely the two diseases may resemble each other is illustrated by the following cases:

Case I (Phipps Institute, No. 9485).—Female, aged twenty-eight years, first came to the Phipps Institute June 10, 1911. Her first pregnancy had resulted in a miscarriage. She gave a history of having had repeated attacks of blood-spitting for five years. During the two years prior to her coming to the dispensary she had lost thirty pounds in weight, and for a year had had a cough, considerable greenish expectoration, and night sweats. She also complained of pain posteriorly over the base of the right lung. There was a slight elevation of temperature, 99° to 100° F.

Examination. There was some flattening beneath the right clavicle, diminished expansion, impairment of resonance on percussion, and bronchovesicular breathing.

She was sent to a sanatorium and remained away for several months, where she gained about sixteen pounds in weight, but the pulmonary symptoms remained unchanged. On her return to the Phipps Institute her sputum was repeatedly examined for tubercle bacilli as well as other organisms, but always with a negative result.

Guinea-pigs inoculated with her sputum were killed after an interval of several months, and showed no evidence of tuberculosis. At the end of ten months her condition, aside from some gain in weight, was about the same as when first seen. A Wassermann test taken at this time was strongly positive. She was then given salvarsan, followed by mixed treatment, which was continued for months. Following the salvarsan the symptoms at once began to improve, and she has apparently made a complete recovery. Three subsequent Wassermann tests have been negative. During the past year she has given birth to a healthy child. At the present time (May 15, 1915) she weighs 188 pounds, and is entirely free from pulmonary symptoms.

Case II (Phipps Institute, No. 9617).—Male, aged thirty-three years, husband of the previous case. First visited the Phipps Institute July 6, 1911, stating that he had had a cough and greenish-colored expectoration for the past two years. He also complained of pain posteriorly over the base of the right lung. He had lost weight and had a slight elevation of temperature in the afternoon.

Examination. Patient was quite anemic. Expansion was diminished beneath the right clavicle, the percussion note was impaired, and the breathing bronchovesicular, with a harsh, prolonged expiratory sound.

He was also sent to a sanatorium, and remained away for six months. Although he gained forty pounds in weight the pulmonary symptoms persisted, and in addition his sputum was blood-streaked at times. On his return to the Phipps Institute his sputum was repeatedly examined for tubercle bacilli and other organisms and also inoculated into guinea-pigs, but with negative results. A Wassermann test taken about a year from his first visit was found to be strongly positive. The administration of salvarsan and later mixed treatment caused a disappearance of his pulmonary symptoms. At the present time (May 15, 1915) he is apparently in perfect health.

Case III (Phipps Institute, No. 4050).—Male, aged twenty-nine years, was first seen in the dispensary of the Phipps Institute April 7, 1906. He came because of loss of weight, dyspnea on exertion, and morning cough and expectoration. On several occasions the sputum had been blood-streaked.

The family history was negative. He admitted having had gonorrhea eight years previously, but denied ever having had syphilis.

Examination. When first seen there were fine crackling rales at both apices, but otherwise the pulmonary signs were negative. The heart was normal. The sputum was negative.

This patient was seen at intervals during the next two years, and for a period of two months, in 1908, was treated in the wards of the Institute. During his stay in the hospital the temperature chart showed frequent elevations, ranging from 99° to 99.3° F. While in the hospital he was given three injections of tuberculin. Following the third injection of 10 mg. there was a slight elevation of temperature. While his symptoms and general condition remained unchanged the rales at the apices had disappeared. The sputum continued to be negative for tubercle bacilli. On leaving the hospital he returned to the dispensary on several occasions, and then ceased to come. After an interval of four years he again reported March 30, 1915. His weight was the same as when last seen. He still had slight fever, and the morning cough and expectoration persisted. In addition he complained of nocturnal pain in his arms and hands and attacks of substernal pain and dyspnea. He had been married about a year when first seen in 1906. In the intervening nine years his wife had given birth to six healthy children.

The physical examination at this time showed no abnormality in the lungs. There was, however, a diastolic murmur at the aortic area. Believing this to be syphilitic in character a Wassermann test was made, which proved to be strongly positive. This case is of special interest because of the long duration of the pulmonary symptoms and the latent character of the trouble.

Case IV (Phipps Institute, No. 13391).—Female, aged thirty-four years, first visited the Phipps Institute August 20, 1914. Her family history was negative. She had been married eleven years and had had three miscarriages. No living children. There was no history of an initial lesion or of secondaries. She came to the dispensary because of a cough, greenish-colored expectoration, night sweats and some loss in weight. In addition she complained of precordial pain, which had been present intermittently for six years. For four years she had suffered from attacks of burning and tingling in the legs.

Examination. Some flattening beneath the right clavicle, impairment of the percussion note, and bronchovesicular breathing. Heart was negative. The reflexes were exaggerated.

During the first six months she was under observation the night sweats, morning cough, and expectoration persisted, and the sputum was blood-tinged on one occasion. There was also a slight rise in temperature. The sputum was negative for tubercle bacilli. In February, 1915, she first complained of nocturnal headache. This gradually became worse, and finally was so severe as to interfere with her sleep. The Wassermann test was strongly positive. Under mixed treatment the headache was relieved. Later, following the administration of salvarsan, the cough ceased and the amount of expectoration was greatly reduced.

Case V (seen in consultation).—This patient was a young male who, when first seen, had been gradually losing weight for three months; during this time he had a slight, hacking, and unproductive cough. He was anemic, had a slight afternoon rise in temperature, and in addition had marked malaise.

EXAMINATION. At the right apex there was slight diminution in expansion, some impairment of the percussion note, and a feeble respiratory murmur.

The case seemed to be clearly one of incipient pulmonary tuberculosis, and he was accordingly advised to spend the winter at a health resort. He returned six months later with his general health improved in every way, but in the course of a few months his symptoms began to return. At this time his physician noted that the sternal end of the right clavicle was enlarged and tender. The Wassermann test was positive. After two doses of salvarsan he had no further trouble, and has remained well during the past three or four years.

It is to be noted that the symptoms in all of these cases were characteristic of pulmonary tuberculosis, namely, morning cough and expectoration, blood-streaked sputum, loss of weight, and a slight elevation of the temperature. In two there was pain resembling that occurring in pleurisy at the base of the right lung. Furthermore, they all had physical signs indicative of incipient tuberculosis.

Some years ago E. G. Janeway[1] pointed out that when the viscera became involved during the tertiary stage of syphilis there is apt to be a moderate amount of fever, a loss of weight, and night sweats. Furthermore, a careful physical examination will often reveal some other noticeable evidence of syphilis, such as enlargement and tenderness of the ribs, clavicles or tibiæ, or an enlarged or indurated testicle. Warthin[2] has emphasized the fact that next to the aorta and heart the testes are the most frequent sites of a syphilitic infection. In a pathological study of 36 cases of syphilis occurring in males, the majority of which were latent and unrecognized during life, an orchitis fibrosa was present in 31. In the case of women a history of miscarriages is extremely significant.

If the lungs are involved there is, in addition to the symptoms mentioned above, cough, which may be dry and unproductive or accompanied by a moderate amount of greenish or yellowish expectoration. Blood-streaked sputum may also occur. Pain at the base of the right lung is not infrequent and may be misinterpreted; it is usually due to a syphilitic perihepatitis and not to pleural inflammation.

The presence of latent syphilis of the lung is to be suspected if in addition to pulmonary symptoms there are present elsewhere in the body lesions which are in all probability luetic in nature, such as a periostitis, orchitis, iritis, or suspicious throat lesions. The recognition of these cases should be relatively easy.

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[1] Trans. Assoc. Amer. Phys., 1898.

[2] Ibid., 1914.

The type of the disease which offers the most difficulty, and which for the most part, escapes detection, is that in which the symptoms are entirely pulmonary and in which there are no associated syphilitic lesions. The 5 cases we have reported were of this type. In 2 (Case I and II) we were unable at any time to detect manifestations of the disease in other parts of the body. In the other three the clinical picture in the beginning was that of tuberculosis, but the subsequent appearance of an aortitis (Case III), of nocturnal headaches (Case IV), of an osteoperiostitis (Case V), and the presence of a positive Wassermann reaction made it apparent that we had to deal with syphilis rather than with tuberculosis. The correctness of this assumption received additional confirmation in view of the fact that the symptoms were relieved as the result of the administration of antisyphilitic treatment.

The diagnosis must be made by exclusion. Thus if the symptoms and physical signs are those characteristic of tuberculosis and the sputum does not contain tubercle bacilli, or the progress of the case differs from that usually encountered in tuberculosis, the possibility of some other exciting cause should be thought of. Not only should the sputum be examined for organisms other than the tubercle bacillus, but in addition a Wassermann test should be made in every doubtful case.

The therapeutic results in these cases have been specially gratifying. In 4 the use of salvarsan was followed by an almost immediate relief of the symptoms. The remaining case has not been seen since the administration of that drug.

It is now recognized that salvarsan is much more effective in some forms of syphilis than it is in others. Skin lesions, for instance, clear up rapidly under the use of salvarsan, and the same seems to be true of pulmonary lesions.

CERTAIN PHYSICAL SIGNS REFERABLE TO THE DIAPHRAGM AND THEIR IMPORTANCE IN DIAGNOSIS.[1]

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The diaphragm, situated as it is in close relation to the intrathoracic viscera and to the upper abdomen, is involved often in abnormal conditions of the organs either immediately above or below it. These conditions frequently exert a distinct effect on the physiological functions of the diaphragm, which in many cases give rise to certain definite physical signs, and are of aid in interpreting the often obscure underlying pathological processes.

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[1] Read before the Mississippi Valley Medical Association at Cincinnati, Ohio, October 27, 1914.

A number of cases in which involvement of the diaphragm was of considerable aid in the eventual diagnosis have come under my observation during the past year. It is the purpose of this paper to briefly review the present-day ideas as to the action of the diaphragm in diseased conditions of the surrounding organs, and to illustrate the importance of some of the resulting physical signs by reports of the cases in which these signs appeared.

Conditions which involve the diaphragm may be broadly divided into two classes: (1) those which through irritation or inflammation of the pleural or peritoneal covering of the diaphragm give rise to a chain of symptoms which depend on the innervation of the diaphragm for their genesis, and (2) those which are caused by changes in the position of the diaphragm, which place the diaphragm at a greater or less mechanical advantage to perform its function.

The pleural and peritoneal coverings of the diaphragm are supplied by the phrenic nerves and the sixth to twelfth intercostal nerves. The outer rim, a space about three inches broad, is supplied by the lower intercostal nerves, while the remaining central portion is innervated by the phrenic nerves.

It has long been known that irritation of the pleural covering of the diaphragm often results in pain and tenderness over the phrenic nerves in the neck, and that this irritation is occasionally accompanied by tender points in the hypochondria. De Mussy[2] was the first to describe these points of tenderness, and they are still referred to as "De Mussy's buttons." Pain or tenderness in the immediate region of the diaphragm has not been noted in such cases. This would suggest that the pleural or peritoneal surfaces of the diaphragm when irritated give rise to pain referred along their nerves to the surface, after the manner of the viscero-sensory reflexes described by Head[3] and MacKenzie.[4] This is further substantiated by observations of MacKenzie[5] and Capps[6], who showed that irritation of the pleural surface of the diaphragm caused no local sensation of pain in the structure.

In 1911 Capps[7] reported a series of ingenious observations on the distribution of the pain sensation which occurred when the pleural surface of the diaphragm was irritated. In a number of cases of pleurisy with effusion, which required paracentesis, Capps inserted a long, blunt wire through the needle before any fluid had been drawn off. In this way he was able to make pressure on different parts of the diaphragmatic pleura and to observe the distribution of the painful sensations which resulted from this procedure. He found that pressure over the surface of the diaphragm caused painful sensations in areas remote from the point of irritation. He further found that these painful areas bore a constant relation to the portion of the diaphragm on which pressure was exerted. When pressure was made on the outer edge of the diaphragm there resulted a sensation of pain in the abdomen, in the flank, or in the lower thorax. On the other hand, when the central portion of the diaphragm was irritated, pain appeared along the ridge of the trapezius muscle or in the shoulder. These painful areas were frequently associated with hyperesthesia or hyperalgesia of the skin and with tenderness on pressure over these points.

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[2] Archiv. Gén. de Méd., Paris, 1853, ii, 271.

[3] Brain, 1893, xvi, 1; ibid., 1894, xvii, 339; ibid., 1896, xix, 153.

[4] Symptoms and Their Interpretation, 1913, p. 71.

[5] Ibid., p. 215.

[6] Archiv. Int. Med., 1911, viii, 717.

[7] Loc. cit.

The following cases will serve to illustrate the symptoms which occur with irritation of the pleural covering of the diaphragm:

Case I.—H. C., male, aged forty-four years, was admitted to the Cleveland City Hospital on November 27, 1912. His family and past history were not important. On the day previous to admission he was seized with a sharp pain in the abdomen. The pain was most marked in the left upper quadrant, but was general over the left side of the abdomen, and was referred to the left flank as well. He vomited once; there was no blood in the vomitus.

When seen the patient was evidently in considerable pain. The heart and lungs were not remarkable, except that there were a few coarse, dry rales throughout both lungs. The excursion at both bases was good and there was a Litten's sign on each side. Deep inspiration seemed to increase the abdominal pain somewhat. There was tenderness over the whole left side of the abdomen, which was more marked in the upper quadrant, at which point there was slight spasm of the muscles on pressure. The temperature was 100° F. The respirations were 22 per minute. The pulse was 70. The urine showed no abnormalities. The white-blood cell count was 28,000.

On the day after admission the patient began to hiccough. The abdominal pain was still severe and the pain in the left flank persisted. The hiccough naturally suggested irritation of the phrenic nerve, but, on account of the distribution of the symptoms, it was deemed probable that the cause of the trouble lay beneath the diaphragm.

On the third day after admission it was noted that in addition to the tenderness there were definite hyperesthesia and hyperalgesia over the left upper quadrant of the abdomen. The patient continued to hiccough constantly. No further signs could be detected in the lungs. During the next two days the hiccough continued, though the abdominal pain entirely abated.

Six days after admission it was noted that pressure over the left phrenic nerve in the neck caused great pain, and that pinching the skin over the ridge of the left trapezius muscle also was very painful. There was no skin hyperesthesia. On this day the temperature, which had ranged between 100° and 102° F., since admission, became normal. The leukocyte count was 7500.

The pain and tenderness in the neck remained for twenty-four hours and then disappeared. The patient continued to hiccough almost constantly until the ninth day of his stay in the hospital.

On the tenth day the temperature rose again to 101.5° F., and the patient complained of pain in the right side of the abdomen, which was accompanied with tenderness in the right upper quadrant. There was also tenderness over the right phrenic nerve in the neck. The white-blood cell count was 16,000.

On the eleventh day a circumscribed friction rub was heard at the right base posteriorly. From then on the symptoms abated and the patient made a rapid recovery.

In this case the onset and early course of the condition strongly suggested an acute abdominal process. The development of uncontrollable hiccough pointed to irritation of the diaphragm, but at first the presumption was that the inflammation was below the diaphragm rather than above it, especially in the absence of any evidence of lung involvement. The appearance of the pain and tenderness over the phrenic nerve in the neck, along with the pain and tenderness and hyperalgesia of the skin over the ridge of the left trapezius muscle, pointed to an irritation of the central portion of the diaphragm. Irritation of the outer rim of the diaphragm, causing painful sensations in the lower dorsal segments, could account for the pain and tenderness in the left hypochondrium. The diagnosis was amply substantiated, it seems to me, by the appearance of a similar though not so well-marked chain of symptoms on the right side, accompanied as they were by a friction rub. It is especially interesting that at no time were there any signs even remotely suggesting the presence of a pulmonary infiltration.

Case II.—E. R., female, aged twenty-two years, was admitted to the Cleveland City Hospital on November 20, 1913. She complained of vomiting and abdominal pain. The patient was in the third month of pregnancy. A few days before admission to the hospital she began to have pain on the right side of the abdomen, had been feverish, and had begun to cough. Physical examination showed a well-developed and nourished young woman. There was slight dulness at the base of the right lung, below the angle of the scapula. The excursion of the lung was somewhat limited on the right. The fremitus was slightly increased at the right base. There were a number of fine crackling rales over the right lower lobe posteriorly, with a somewhat prolonged expiration. The subcostal angle moved normally.

The abdomen was soft everywhere. There was no rigidity and no masses were palpable. The right upper quadrant was uniformly tender on pressure, and the skin of this region showed marked hyperesthesia and hyperalgesia. Examination of the cardiovascular system showed nothing abnormal.

The ridge of the right trapezius muscle was very tender, and the skin over this area was distinctly hyperesthetic. The patient hiccoughed frequently during the examination.

The temperature was 100° F. The respirations were 26. The pulse was 110. The urine was negative. The leukocyte count was 19,600.

Further observation on this case was not possible, as she left the hospital against advice, with the condition practically unchanged.

In this case the physical signs indicated an involvement of the lower lobe of the right lung. In the presence of abdominal pain, tenderness, and hyperesthesia of the skin, as well as of pain and of tenderness along the ridge of the right trapezius muscle, it is reasonable to suppose that an inflammation of the diaphragmatic pleura existed.

In the light of the above cases Capps'[8] observations on 19 cases of diaphragmatic pleurisy are of interest. Out of 19 cases he found that 8 had pain in the abdomen as far down as the navel, and that in 11 cases the pain extended all over one-half of the abdomen. The pain was spontaneous, but was associated with tenderness on pressure. It has been my experience in such cases that the tenderness on pressure over the abdomen is due to cutaneous hyperesthesia. In 11 out of the 19 cases he found pain over the ridge of the trapezius muscle or on the side of the neck, usually associated with hyperesthesia of the skin.

In these cases of inflammation of the diaphragmatic pleura the distribution of pain is either along the phrenic nerve, and is made evident in the third and fourth cervical segments, or along the sixth to twelfth intercostal nerves, with a distribution in the lower dorsal segments, substantiating the view that the pain sensations resulting from irritation of the serous covering of the diaphragm is a true viscero-sensory reflex.

In order to understand the effect of change of position of the diaphragm a brief review of its actions is necessary. During inspiration the contraction of the diaphragm increases the vertical diameter of the thorax. The diaphragm descends a certain distance and withdraws from the chest walls in the regions of the pulmonary sinuses allowing the inflated lungs to descend. The older conception that the diaphragm forces the organs immediately below it downward, with a piston-like motion, is probably not tenable at present. The scalene muscles and the intercostals lift the ribs during inspiration which action results in drawing the costal borders away from the median line, or in other words, in a widening of the subcostal angle. The contraction of the diaphragm, besides increasing the vertical diameter of the thorax, will also tend toward an inward pull along its line of attachment especially along the anterior and lateral insertions which will be in direct antagonism to the outward flaring of the subcostal angle, caused by the action of the scalene and intercostal muscles.

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[8] Loc. cit.

Hoover[9] has demonstrated the presence of this antagonism very conclusively. When the diaphragm of a dog was stimulated with a strong electric current, causing a marked contraction, the subcostal angle was seen to be drawn sharply toward the median line. On the other hand, when the roots of the phrenic nerves on both sides were cut, resulting in complete paralysis of the diaphragm, the inspiratory flaring of the subcostal angle was very much increased over the normal.

Now if for any reason the diaphragm assumes a lower position than normal, especially in its anterior portion, the pull of its inspiratory contraction will be exerted more directly on its points of insertion, which will place the diaphragm at a greater mechanical advantage and will give it the power to equalize or overcome the outward pull of the scalenes and intercostals. This will result in an abolition of the normal flaring of the subcostal angle, or in an actual narrowing of the angle with a movement toward the median line instead of away from it. On the other hand, conditions which displace the diaphragm upward will accentuate the normal upward curve of the diaphragm, with a resulting diminution in its ability to pull against the muscles which raise the thorax and cause the normal outward movement of the subcostal angle.

Hoover[10] has shown experimentally that changes in position of the diaphragm will have these effects on its pulling power, and he has further shown that in certain diseased conditions which alter the position of the diaphragm in an upward or downward direction the movements of the subcostal angle may be of distinct diagnostic assistance.

While very marked retractions of the subcostal angle on inspiration may be plainly visible, it is often impossible to determine whether the retraction is present without the use of palpation. The best method of palpation is to place the thumbs along the line of the costal margin, pointing toward the ensiform cartilage, and have the patient breathe deeply. Slight limitations of motion or slight retractions of the angle are then readily appreciated. This is especially necessary in fat persons, or in persons in whom the respiratory movements are generally diminished.

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[9] Archiv. Int. Med., 1913, xii, 214.

[10] Loc. cit.

I have observed a number of cases in which the position of the diaphragm affected the movements, some of the more interesting of which I wish to discuss:

Case I.—S. A., male, entered the hospital with a low-grade infiltration of the base of the right lung. He had a chronic nephritis with some edema of the extremities. His heart was not remarkable at admission, but in a few days the area of cardiac dulness began to increase to the left and right. The heart sounds became more distant daily. There was no blunting of the cardiohepatic angle, and no change in dulness or change of position. There was no paradoxical pulse. On inspiration the costal margin on the left definitely approached the median line, while that on the right swung out in the usual manner. The left lung and pleural cavity were clear. During the next twenty-four hours the cardiac dulness continued to extend to left and to right. The left border of cardiac dulness reached nearly to the anterior axillary line. The retraction on the left became more marked as the cardiac dulness increased. An exploratory puncture of the pericardium showed the presence of a clear, straw-colored fluid in the pericardial sac and some 100 c.c. of fluid were removed. On the removal of the fluid the area of cardiac dulness returned to normal and the retraction of the costal margin disappeared.

The pericardium filled up again twice with a repetition of the same signs, which disappeared at once after the fluid in the pericardium was removed again.

Case II.—R. N., was admitted to the hospital suffering from severe myocardial decompensation, with edema of the legs, enlarged and tender liver, shortness of breath, and orthopnea. The heart's action was weak and irregular, and there was considerable enlargement of the cardiac dulness both to left and to right. There was no retraction of the subcostal angle. Under rest and digitalis the symptoms rapidly abated, the edema left his legs, and the heart dulness returned almost to the normal size. The pulse slowed and became regular. During a routine examination of the heart a few days later it was found that the cardiac dulness had again increased in size, especially to the left, and that there was apparently a distinct blunting of the cardiohepatic angle. It was noted that there was now a distinct retraction of the left costal margin. Both chest cavities were clear. The patient was perfectly comfortable and lay flat in bed. The cardiac dulness continued to increase in size and the retraction of the left costal margin to become more marked. Roentgen-ray picture taken at this time showed a large pear-shaped shadow of the heart area, which was much denser than the usual cardiac shadow. After a few days the above-mentioned signs began slowly to retreat. The dulness became less in size until it reached the normal, and the retraction coincidentally became less until it disappeared entirely, giving place to a normal movement of the subcostal angle. A Roentgen-ray picture taken at this time showed a heart normal in size, the difference in the two pictures being very striking. In the absence of any signs of cardiac embarrassment, taken with the rapid change in the signs, also with the rapid diminution in the size of the heart shadow, it is reasonable to suppose that we were dealing with an effusion into the pericardium, though no exploratory puncture was made.

In these two cases the pericardial sac was filled with fluid. The weight of this fluid depressed the diaphragm on the left side, especially in its anterior portion, bringing that part of the diaphragm lower and giving it a greater mechanical advantage, which resulted in a pull strong enough to overcome the intercostals and scalenes, and therefore caused a retraction of the subcostal angle on the left.

I have observed several cases of cardiac decompensation with great enlargement of the right heart, wherein there has been slight retraction of the left costal margin. The effect on the diaphragm of the enlarged right heart will be the same as that of an overfilled pericardium, but to a less degree. In my experience the retractions occurring with dilatation of the right heart are never so marked nor so constant as in the two cases of pericardial effusion cited above.

In pneumothorax and in pleurisy with effusion where there are no adhesions the depression of the diaphragm will result in retraction of the subcostal angle. In two cases of pneumothorax the retraction has been very definite. It has been present in practically all cases of fresh pleurisy with effusion which I have seen in the last twelve months at the Cleveland City Hospital, even when the effusions were small in amount.

Fluid may, when encapsulated by adhesions, however, be present in a considerable amount without the presence of a retraction of a subcostal angle. The following case illustrates this point:

Case III.—R. B., two days before admission to hospital, had had sharp pain in the right side of the chest, accompanied by chill. On admission, examination of the lungs revealed slight dulness in the right axilla with a few crackles and slight tubular breathing. There was decided tenderness over the skin along the ridge of the right trapezius and over the right phrenic nerve in the neck, and also tenderness and hyperesthesia of the skin in the right hypochondrium. Slowly signs of fluid appeared at the right base posteriorly, which continued to increase. The anterior border of the flatness extended only to the midaxillary line. Examination of the anterior portion of the chest showed no signs of fluid. There was no retraction of the right costal margin, though signs of fluid continued to increase posteriorly. On tapping a pint of fluid was removed.

In this case the signs of fluid were confined to the posterior portion of the chest, and the history and the signs on admission suggest the presence of an acute fibrinous pleurisy of the diaphragm and parietal pleura. Probably on account of this the fluid was held in a limited portion of the pleural cavity and therefore could not get forward far enough to depress the anterior portion of the diaphragm. This would explain the absence of retraction of the subcostal angle in this case, even though there was a considerable accumulation of fluid in the pleural cavity.

Certain cases of old adhesive pleuritis will show a marked retraction of the costal margin on the affected side during inspiration. I have observed several such cases. It is presumable that in this condition the pleural sinus is obliterated and that the diaphragm acquired what amounts to a much higher attachment than normal. In these cases the pull of the diaphragm when it contracts will be more direct, and will, therefore, be more powerful than normal, and will result in a retraction of the costal margin.

In contradistinction to the above class of cases are those in which the diaphragm is pushed up from below so that the pull of its contraction is less than usual. This will increase the advantage of the scalene and intercostal muscles, and will result in an increased outward movement of the subcostal angle. This is frequently seen in enlargements of the liver or spleen, but is probably most important in large collections of fluid below the diaphragm. In large subdiaphragmatic abscesses the signs often simulate those of fluid within the pleural cavity, except that there will be an increased flaring of the costal margin on the affected side on account of the accumulation of pus below the diaphragm. Hoover[11] reports two cases in which the differential diagnosis between empyema and subdiaphragmatic abscess rested entirely on the increased outward movement of the subcostal angle. Subsequent operation in both cases proved the diagnosis to have been correct.

SUMMARY. 1. Inflammation or irritation of the pleural or peritoneal surface of the diaphragm does not give rise to local symptoms. The pain resulting from such processes is referred upward along the phrenic nerves to the third or fourth cervical segments or downward along the sixth to twelfth intercostals into the lower dorsal segments. The pain is usually accompanied by tenderness and hyperesthesia or hyperalgesia of the skin. The recognition and interpretation of these signs may be of considerable importance in differential diagnosis between intrathoracic or intraperitoneal disease, in the absence of any signs in the lungs.

2. When the part or the whole of the diaphragm is forced downward the contraction of the diaphragm exerts a more powerful inward pull along the line of its attachments. This is especially marked when the anterior portion of the diaphragm is depressed. This will result in a lessening of the outward excursion of the subcostal angle, or an actual retraction along the line of diaphragmatic attachment. Conversely any condition which lifts the diaphragm upward lessens the strength of the inward pull of the contracting

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[11] Loc. cit.

diaphragm, with the result that the normal outward movement of the costal margins will be increased.

3. The presence of a retraction or of an abnormal outward flaring of the subcostal angle will often be of aid in the explanation of obscure diseases of the viscera which lie immediately above or immediately below the diaphragm, especially in pericardial effusion or in subphrenic abscess.

PLEURISY.

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Pleurisy in one of its many forms is the commonest of the diseases of the chest, and the most unmanageable. It is often less easy of successful treatment than pneumonia, and sometimes leaves behind it more permanent mischief. Slight attacks may occur without being recognized, explaining the frequency of pleuritic adhesions found in the postmortem examinations of persons who were never known to have been ill. It occurs at all ages, from early infancy to advancing years, but is more frequent in the male between youth and middle age. Its etiological data, bacterial or general, are not, in our present knowledge, quite well enough understood to establish a definite classification. The disease is usually one-sided, preferably confined to the right, though occasionally it is bilateral, and then is apt to be secondary to phthisis or septicemia. It is primary or secondary. By the term primary is meant inflammation of the pleura in a time of health, being mainly limited to the membrane itself, with secondary constitutional results of fever, or if exudation be present, to the mechanical effects of pressure in addition. Secondary pleurisies are by far the more common and the more serious, associated as they so often are with disease of the lungs or neighboring viscera, and sometimes complicating infective processes in the body.

Pleurisies are also divided into the acute and chronic, based upon clinical symptoms, often found, however, to be of doubtful significance. The chronic is frequently of that form from the onset, but it is more likely to be consecutive to the acute. The chief varieties of pleurisy are the fibrinous, the serofibrinous, and the purulent. The predominant causative bacteria are the tubercle bacilli, the pneumococci, and the streptococci. The exudates are often found to be sterile and when a purulent exudate is sterile it is invariably tuberculous. Bacilli of lesser importance exist in the mixed forms.

Fibrinous or plastic pleurisy is often confined to a circumscribed area, lasting for a few days and terminating by adhesions. Its friction sound is not propagated, but dies where it was born and may readily escape detection. Diffused spots of subacute inflammation not uncommonly occur in connection with chronic nephritis, and if there be friction in the cardiac region it may be influenced by the rhythm of the heart as well as by respiration.

Chronic dry pleurisy, which is usually tuberculous, has in many instances an acute onset, causing thickening of the pleura, extensive adhesions, and fibrosis of cortical portions of the lung. It may remain localized for months or even for years, finally proving fatal from pulmonary phthisis or from acute miliary tuberculosis. I have known of a case of extensive plastic pleurisy of many years' duration to terminate fatally from pneumothorax. The autopsy revealed extensive adhesions binding the lung posteriorly from base to apex. The non-adherent portions of the lung were compressed backward by accumulated air from a ruptured tuberculous ulcer. The pleural cavity was practically free from liquid.

Acute fibroserous pleurisy attacking one in apparent good health after exposure to cold or possibly to traumatism begins with a chill or usually a sense of chilliness, stabbing pain in the chest, disturbed breathing, and fever. A pronounced chill occurs less frequently in pleurisy than in pneumonia, algid attacks taking the place of the former at irregular intervals during the first few days. Pain, on the contrary, is usually intense in pleurisy. It is lancinating, as if from the thrust of a sharp instrument, and often makes the patient cry out on taking a deep breath or after a cough. It is also increased by pressure and by movements of the body.

The pain lessens or ceases altogether when adhesions occur, or when the inflamed surfaces of the pleura are separated by liquid effusion, though it may return intermittingly during the patient's illness from exacerbations of the original attack. The seat of election of pleuritic pain is a few fingers' breadth below the nipple, though its point of maximum intensity may be elsewhere in the lateral region of the chest or posteriorly below the inferior angle of the scapula. Occasionally the pain is referred to the lower dorsal region or to some part of the abdomen, giving rise, in the absence of careful examination of the chest, to grave errors in diagnosis. I have known of two patients suffering from pain in the abdomen, one a girl of five years, the other a man about forty years, to be operated upon, the one for appendicitis, the other for perforated gastric ulcer. Both cases ended fatally, showing at the autopsy double serofibrinous pleurisy in the child, and localized diaphragmatic pleurisy in the man. The different seats of pain do not throw clear light upon the precise localization of the disease or its extent, but merely indicate the side affected. Sometimes, however, the pain of circumscribed pleurisy corresponds exactly with the seat of inflammation. In double pleurisy, pain is often felt on one side alone or it may be confined to the middle of the thorax. It is rarely itself double, but may change from one side to the other, according to the progress of the disease, each one of the pleuræ being successively involved.

The respirations at first are always embarrassed and painful in consequence of efforts at full breathing, the inspiration being cut short before it is completed. But there is not true dyspnea until the lung is compressed by effusion, and perhaps not then unless it be rapid and copious. Cough is sometimes wanting, but in the majority of cases the patient has a short, dry, shallow cough with attempts at restraint, because of the pain to which it gives rise. It is occasionally attended with scanty expectoration of thin, frothy mucus, but if it be abundant and opaque, an association with bronchitis or other affection of the lung is found to exist. In recent cases of moderate severity the pulse bears a close relation to the height of the fever, and is not greatly in excess of the normal. In cases of large effusion with sudden compression of the lung there is a disturbed balance between the pulmonary and general circulation, sufficient blood not passing from the right ventricle into the lungs, and through them to the left side of the heart and the arterial system. Under these circumstances the action of the heart is violent and the pulse at the wrist is frequent and repressed to such a degree as to cause danger from suffocation.

A young man under my care, laboring under an acute pleuritic attack with large effusion, left his bed in the absence of the nurse and walked some distance to the end of the room, the exertion proving almost fatal. On his return to bed the patient was gasping for breath, his heart was beating violently, and his pulse was indicative of lowered arterial tension. Venesection was followed by prompt relief to the threatening symptoms.

The fever of acute pleurisy is of remittent type, with exacerbations toward evening, lasting until the exudate reaches its maximum, when it gradually declines without an attempt on the part of nature to promote a crisis. In some cases the fever returns at irregular intervals, but it finally drops to the normal. Should the temperature be persistently elevated and intermittent there is every reason to suspect the existence of pus in the pleural cavity.

The decubitus of the patient suffering from pleurisy is frequently changed during the course of the malady. At the onset, when there is pain and tenderness on pressure, while the patient avoids lying directly on the affected side, his body is often inclined in that direction. Late in the disease he assumes the dorsal decubitus, but when the effusion is very great the patient naturally prefers lying on the diseased side to relieve the healthy lung of the weight of the fluid. The duration of the active symptoms of acute primary pleurisy with moderate effusion is from ten to twenty days, when absorption begins progressing slowly, however, before the process is completed, often lasting for many weeks. Retraction of portions of the chest, impairment of resonance, and feebleness of breath sounds with coarse friction may exist for an indefinite length of time, the patient being able to walk about, though looking ill and suffering from dyspnea on exertion.

Chronic pleurisy, as a rule, is the continuation of the acute, though it may result from some low-grade infection from the beginning, in which case the greater number are secondary to a constitutional malady or to some visceral disease. The affection sometimes exists in the form of what is termed latent pleurisy, without any of the general symptoms, unless dyspnea be present, and yet one side of the chest is found to be largely filled with fluid. The physical signs alone reveal the disease, and in every case of suspected infection of the chest a careful examination should always be made.

The following case is mentioned to show how a person laboring under pleurisy of chronic form with enormous effusion was able to perform the full duties of his position without much inconvenience:

C. L., a Chinaman by birth, and cook in a private family, aged sixty-six years, was admitted into the Bryn Mawr Hospital on April 1, 1914. He had been troubled with cough, slight pain in the right side, and shortness of breath for about four weeks, but did not give up work until the day of his admission. On examination the right side of his chest was found to be distended, and there was scarcely any perceptible movement during respiration. There was flatness on percussion and absence of vocal vibrations from three inches below the clavicle in front and below the spine of the scapula posteriorly. At the apex of the lung front and back the percussion note was high-pitched and tympanitic. The breath sounds were altogether absent in the dull regions. Above the level of the fluid posteriorly, and near the spinal column over the compressed lung, there was bronchial respiration and bronchophony. The heart was not much displaced. On April 3, the effusion was so great that the whole of the right side of the chest was absolutely dull on percussion, and breath sounds were everywhere absent except at the root of the lung. Aspiration of the chest was performed, with the result of removing 2200 c.c. of serous fluid, afterward found to be sterile. The patient left the hospital April 23 much improved in health, but suffered a relapse and was readmitted on May 3. The right chest had already undergone retraction. There was dulness posteriorly below the angle of the scapula, and the breath sounds were harsh and distant. Elsewhere on the right side there was tympanitic dulness on percussion and an approach to bronchial breathing. On July 3 the patient was discharged for the second time, with the view of being sent to a sanitarium for outdoor treatment.

Two boys under my care were also cases of latent pleurisy, the first, aged ten years, had passed a section of tape-worm shortly before my visit, and I found him in bed suffering from abdominal pain, naturally attributed to the irritation of the parasite. There was an absence of symptoms referable to the chest except slight dyspnea, which led me to discover that the patient's left pleural cavity was more than half filled with fluid. The second boy, aged five years, was brought to the country to recover from a gastric attack. He had slight fever, epigastric tenderness, nausea, and vomiting. On examining his chest I found a large effusion on the right side, with all of the characteristic physical signs of pleural inflammation. Both of these patients made good recoveries.

A remarkable instance of pleurisy without marked symptoms was that of Mrs. R., aged forty-five years, who when I first saw her was up and about attending to her household affairs. I was informed that she had been indisposed for a week or more, that she had occasional cough but without pain, and was feverish at night. Examination of the chest revealed dulness on percussion, with absence of breath sounds and of vocal fremitus over the whole of the right lung. There was entire absence of movement of the right side of the chest during respiration, the intercostal spaces were bulging, and the adjacent organs displaced. I left the patient's house to arrange for immediate tapping of the chest, and before I had time to return a message was received that sudden death had occurred after the patient's exertion of going up stairs to the second floor.

The modern practice of early thoracentesis has notably lessened sudden death in pleurisy, though it is still occasionally reported. I once knew fatal syncope to occur, at the Bryn Mawr Hospital, during operation for the removal of fluid from the chest of a robust colored man suffering from acute pleurisy. An autopsy was not allowed.

In cases of pleurisy of long standing neglect the chest is sometimes enormously distended and the comparative immobility between the two sides is most remarkable, the patient raising up the sound side while that of the seat of disease is almost quiet. The intercostal spaces are widened, effaced, and sometimes bulging. The nipple is abnormally distant from the central line of the sternum, and I have often observed it elevated. The neighboring viscera are displaced, chief among them being the heart, which is carried far to the opposite side of the chest. After absorption of the fluid or when it has been mechanically removed, atmospheric pressure is found to have pushed in the parietes of the chest toward the unexpanded lung, giving rise to contraction not only in circumference but from above downward, displacing the scapula and obliterating the intercostal spaces by encroachment of the ribs. The shoulder droops and the body inclines to the affected side, giving the patient a peculiar "lob-sided" gait. In a right-sided pleurisy under these circumstances the liver is drawn up and the heart sometimes pulled over to the right, quite the reverse of what happens when effusion exists.

In a chronic pleuritic case coming under earlier observation the lung, though pushed upward toward the mediastinum or spinal fossa, is less adherent and reëxpands more fully when absorption of the fluid takes place, or is withdrawn by aspiration, and therefore retraction of the chest is less marked. Purulent pleurisy occasionally follows injury to the chest with deep-seated lacerations or it is not infrequently secondary to an acute infective disease. Puerperal pleurisy is often purulent, bilateral, and consequently fatal. Primary suppurative pleurisy is extremely rare in the adult. It is almost always serofibrinous at first, becoming purulent during its subsequent course. It is a common disease of infancy and childhood, and in many instances at that period of life it is purulent from the beginning. The general symptoms are not in any particular different from those of serous pleurisy, with the exception of the persistence of fever and its marked evening rise. Before the days of antisepsis there were many errors of diagnosis and a high mortality of empyema, but now exploratory puncture leads to prompt recognition of the disease and immediate operation. Formerly attempts of nature at spontaneous cure were met with by the discharge of pus through a perforated bronchus or by the formation of a subcutaneous abscess in the parietes of the chest communicating with the pleura, *pleuritis necessitatis*.

In 1886 Miss S., aged eighteen years, was under my care, suffering from acute serous pleurisy. On my first visit there was unmistakable evidence of left-sided pleurisy. Effusion took place rapidly and was copious. In the second week two pints of semi-opaque fluid were removed from the pleural cavity by aspiration. Cough was excessively annoying, and was continuously troublesome until the beginning of the fourth week, when after a violent paroxysm the patient expectorated a large quantity of extremely fetid pus. The discharge was brought up after cough, and on changes of position for many weeks. The patient became profoundly hectic and greatly emaciated, but after a prolonged illness recovered. She is now living and in good health.

Another incident of empyema is perforation of the diaphragm and the escape of pus into the peritoneal cavity, causing local or general inflammation. I have known of two such cases, both terminating fatally after operation. One, a young lady, the subject of tuberculous pleurisy of acute onset, with a copious effusion lasting for many weeks before the fluid was appreciably absorbed. In course of time her general health was sufficiently improved to enable her to go to the far west in search of a suitable climate, which was successfully accomplished, with good results. A second attack of pleurisy, however, was soon followed by suppuration, and pus discharged through the diaphragm, causing a walled-off abscess in the right hypochondrium.

My second patient, a saloon-keeper living in the West, aged forty years, was attacked with right-sided pleurisy, the effusion becoming rapidly purulent, perforating the diaphragm, and causing general peritonitis. The disease was far advanced when the patient came under observation, and being an extreme alcoholic, he developed septicemia and died soon after being operated upon.

An incident of extension of infection from below upward was that of John C., aged fifty years, admitted into the Bryn Mawr Hospital on June 23, 1914, having a subphrenic abscess associated with pyopneumothorax, caused by perforation of the diaphragm, establishing a communication between the subdiaphragmatic region and the right pleura. The symptoms were abdominal and thoracic, the former more especially, as shown by a large, painful area of resistance in the hypochondrium. The thoracic symptoms were high-pitched tympanitic resonance over the lower half of the right chest, restriction of movement during respiration, with muffled bronchial and occasionally amphoric breathing posteriorly below the angle of the scapula. The normal liver dulness was replaced by tympanitic resonance on percussion. Under local anesthesia a free vertical incision was made in the right hypochondrium, giving exit to a large quantity of extremely fetid pus containing gas. A counter-opening was made in the dependent part of the abscess to insure free drainage. Several weeks later the chest was opened in the anterior axillary line and the sixth rib resected. The patient recovered and left the hospital on November 23, 1914.

A rare case of pleuritis acutissima of foudroyant type, rapidly becoming empyemic, was recently under my observation at the Bryn Mawr Hospital. Ross P., aged thirty-four years, a teamster, of intemperate habits, was admitted into the Hospital on December 12, 1914. The history he gave was that he took cold from exposure in a rain storm, and was confined to the house for one week before coming to the hospital with a troublesome cough, extreme malaise, and finally a chill and pain in the left side. He was complaining on admission of sharp pain in the left side and difficulty in breathing. He had a high temperature, frequent pulse, and excessive cough, with mucous blood-stained expectoration. The tongue, dryish and brown, was tremulously protruded. He was incoherently delirious, and was inclined to get out of bed. There was dulness on percussion over the lower half of the left lung posteriorly, with absent vocal fremitus, feeble breath sounds, much prolonged expiration, and distinct egophony below the angle of the scapula. On December 13 the patient become violently delirious and jumped out of the window, falling on the ground, a distance of twelve feet, but without sustaining serious injury. The patient's delirium lasted for a week or more with fever going at one time to 105°, and on December 25, on exploratory puncture, the effusion was found to contain pus. Owing to the patient's excitable condition, operation upon the chest was delayed until January 5, 1915, when 600 c.c.

of purulent fluid were evacuated from the chest by incision and resection of one rib. The infection was found to be pneumococcic. The patient is now, January 14 recovering.

Prominent among other varieties of pleurisy depending for the most part upon anatomical conditions are the diaphragmatic, hemorrhagic, interlobar, and the pleuropneumonic.

In restricted pleurisy when the diaphragm is the exclusive seat of the disease the general symptoms are to be mainly relied upon in making a diagnosis. The physical signs are indefinite and often altogether absent. Auscultation sometimes reveals feebleness of the vesicular murmur and a few subcrepitant rales at the base of the lung of the side affected. The attack begins suddenly, preceded by a chill and followed by high fever, violent pain, and excessive dyspnea. The pain is usually referred to the hypochondrium, extending to the epigastrium, and sometimes to the ileolumbar region of the corresponding side. It is increased by deep inspiration, and is made intolerable by hiccough and vomiting. The painful regions are very tender to the lightest touch. This is especially true, as has been pointed out by M. Gueneau de Mussy, of a spot one or two finger's breath from the linia alba on the level with the bony part of the tenth rib. When this point is even slightly pressed upon the patient cries out, and there is also a sudden increase of dyspnea, seeming to threaten suffocation. This spot M. de Mussy called "le bouton diaphragmatique." The phenomenon is explained by a hypersensitive branch of the phrenic nerve. Pressing upon the hypochondrium from below upward also gives rise to great pain. The respirations are excessively frequent and almost convulsive in character. The patient breathes with the ribs rather than with the diaphragm. The difficulty of breathing is sometimes so great as to cause orthopnea, the patient leaning forward and supporting the painful part with the hand to immobilize the chest.

Hemorrhagic pleurisy is of rare occurrence in the primary form. In the majority of instances it is secondary to some organic disease or to a general infection. Its physical signs do not differ practically from those of the serofibrinous variety, and accurate information is only to be obtained by exploratory puncture.

Some years ago a man of middle age, who was under my care suffering from an acute exacerbation of chronic articular gout, was taken with pain in the right side, with rapid filling up of the pleural cavity. He had enlargement of the heart, with long-standing valvular disease and cirrhotic kidneys. On being tapped the pleural effusion was found to be hemorrhagic. Death occurred after a short illness from uremia.

Another patient under my care was a lad, aged eighteen years, of good previous health and about to enter college, who took ill with pyrexia which proved to be typhoid of irregular type. At the beginning of convalescence he was attacked with left-sided pleurisy, followed by a rapid and copious hemorrhagic effusion. The patient after an illness of many weeks finally recovered sufficiently well to get about and retained improved health until several months later, when he was taken suddenly ill with tuberculous meningitis, ending fatally in about ten days.

Interlobar pleurisy with sacculated effusion, serous or purulent, is always difficult to diagnose, and often impossible to locate. It rarely exists alone, but is associated with extensive fibrinous or serofibrinous inflammation. A cystic empyema is the more common, and is sometimes an infection associated with pneumonia. Persistent fever, with increasing evening exacerbations and a high leukocyte count, leads to exploratory puncture, and if purulent fluid be found, operation is called for.

A colored woman, by occupation a cook, under my care a few years ago, was taken ill with pneumonia of the apex of the right lung, beginning with a violent chill and followed by fever, dyspnea, and cough, with rusty sputum, a pseudocrisis occurring on the ninth day of the patient's illness. The fever increased again with marked evening rise, lasting for many weeks. The leukocyte count varied from 17,000 to 24,000. The cough was most annoying, and the expectoration, scanty at first, increased in quantity and became purulent. Repeated exploratory punctures failed to reveal the presence of pus. The physical signs were localized dulness and rough breathing near the original seat of pneumonia, and impairment of resonance from the spine of the scapula to the base of the lung, with coarse friction and bronchovesicular respiration. After an exhausting illness of many months the patient was able to resume her former occupation. The case unquestionably was one of empyema in the fissure between the upper and middle lobe of the right lung, remaining undiscovered by puncture, and finally discharging through a bronchial fistula. Pleurisy and pneumonia are often combined; indeed, pneumonia rarely exists without some degree of plastic inflammation of the pulmonary pleura; but to properly constitute a case of pleuropneumonia there must be a decided effusion. More than the ordinary amount of pain indicates the coexistence of the two diseases, and if there be positive flatness on percussion at the base of the lung, lessened or absent vocal fremitus, indistinctness of bronchial breathing and perhaps egophony, the diagnosis can be no longer in doubt. The convalescence is more apt to end by lysis, and is prolonged by fluid remaining to be absorbed.

The physical signs of pleurisy vary according to the stage of the disease and the amount of effusion in the pleural cavity. Compared with the general symptoms they are of greater importance in forming a correct diagnosis. The expansion of the lower part of the affected side is less than that of the sound side, even before effusion occurs, mainly in consequence of painful breathing, and the corresponding side of the chest is also somewhat retracted as may be shown by measurement.

Palpation is not only of use in determining the degree of lessening of the respiratory movements, but is also of great importance in estimating the strength of the vocal vibrations, which are absent in deep effusions and feebly present in others, a physical sign of much importance from a diagnostic point of view. Palpation is a useful means of determining the degree of displacement of the heart and the extent of downward displacement of abdominal organs. In pleurisy with large effusion on the right side the free edge of the liver is often felt below the costal border, and if the left side be the seat of disease, the outlines of the spleen are sometimes distinctly made out.

The sounds on percussion in pleurisy are the most important of all of the physical signs. At the onset there is no material change, but when effusion occurs it gives rise to dulness on light percussion, becoming gradually flat as the liquid increases in quantity.

Fluid dulness has a character of its own, if percussion be not too strong, being airless without resonance, and different from the dulness of lung-consolidation, not unlike the sound obtained on striking the thigh. The flatness is more decided at the lower portion of the chest and becomes gradually less from below upward. If the disease be left-sided, allowance must be made for the resonance of the stomach, which often modifies the sound as far up as the eighth interspace. As the effusion increases the upper line of dulness when the patient is sitting upright is not horizontal but assumes more or less the shape of an extended letter S, curving upward and forward to the axillary region, thence downward to the lower part of the sternum. The percussion note above the level of a large effusion is dull and tympanitic, and in front below the clavicle it has high-pitched tympanitic or Skodaic resonance of exaggerated intensity, contrasting strongly with the flatness lower down. The depth of the sound and its tympanitic quality is one of the most characteristic signs of pleuritic effusion, extending up as high as the third or fourth rib anteriorly. When the pleural cavity is quite filled with fluid the percussion note is dull everywhere on the side affected, except at the root of the lung, where the bronchial tubes are large and rigid. Under these circumstances, if the disease be on the left side dulness on percussion replaces the normal tympanitic resonance of Traube's semilunar space following depression of the diaphragm, and with it the stomach which lies in close contact. In rare cases of large left-sided effusions the lifting power of the lung may be sufficient to counterbalance the weight of the fluid to the extent of limiting the depression of the diaphragm and not greatly interfering with the tympanitic resonance of Traube's space throughout the attack.

The auscultatory signs of pleurisy vary greatly according to the extent of the inflammation, the amount of effusion, the degree of compression of the lung, and the number of adhesions. The respiratory murmur, somewhat enfeebled at first by restricted movement of the lung from pain, is still more so when liquid effusion occurs. As the effusion takes place the breath sounds become more feeble and rough, with prolonged expiration, which in the lower part of the chest may be altogether absent. Above the level of the fluid, where the compressed lung, still containing air, is in contact with the walls of the chest or only separated by a small amount of liquid, the respiration becomes more or less bronchial, its intensity varying according to the degree of condensation of the lung, and the voice is bronchophonic. Bronchial respiration and bronchophony coexist in pleurisy, but the latter has a vibration or quivering in its tone which never exists, at least to the same degree, in pneumonia proper. When the bronchial respiration is not loud the resonance of the voice becomes less bronchial, but its vibration is increased and so-called egophony is heard.

The sound of egophony is not of much diagnostic importance in pleurisy, because it requires for its production a thin stratum of liquid intervening between the lung and the side of the chest, and therefore a moderate pressure upon the bronchial tubes. The sound ceases entirely when the effusion is large or else it is converted into bronchophony, of which it is merely a modification. The sound has been known to be propagated through a layer of false membrane after the pleural liquid has been withdrawn. It has been called one of the fancy signs of pleurisy. Its full though rare development once heard is never forgotten. The egophonic voice, when it exists, is best heard between the anterior axillary line and the scapula or in the interscapular region of the affected side. It is more frequently heard in women and children because of the higher pitch of their voice.

Another sign of pleurisy more important than the resonance of the voice and pathognomonic of the disease is the friction sound. It is heard both upon inspiration and expiration, more especially the former, and is often irregular from sticking together of the opposed pleural surfaces, which are released by an unusually deep inspiration such as that after cough. The friction sound is most liable to be confounded with a rhoncus, which is itself often perceptible to the touch; but a friction sound is seldom so loud as a rhoncus, and is rather increased by deep inspiration, whereas a rhoncus is altered or ceases after a vigorous cough. It is also characteristic of a friction sound that it is rendered more distinct when firm pressure by the stethoscope or by the ear is made against the chest. Friction occurs under two different circumstances; at the beginning before serum is effused and toward the termination of the disease when the liquid has undergone absorption or has been evacuated by tapping and the two inflamed surfaces of the pleura again come in contact. At the close of the disease it is coarser and louder, and is best heard below the angle of the scapula or in the lateral region of the thorax. One reason why a friction is so often overlooked is because it is a sign rather than a sound, as shown by slight jerking movements of the chest. The character of friction sounds vary from the finest crepitation to the sole-leather friction or "bruit de cuir neuf" sometimes heard at a distance from the patient and often perceptible to the touch. Pleural crepitation occurs in volley form, resembling the crepitant rale of pneumonia, but it is finer, more moist, and is directly under the ear. I have occasionally found it in association with the sounds of catarrhal bronchitis, especially when the patient had violent fits of coughing.

The physical signs of pleurisy in infancy and childhood show great variations and cannot alone be depended upon, but must be compared with the general symptoms and the history of the attack in making a diagnosis. Of the diseases of the chest in children, pleurisy is the disease in which mistakes in diagnosis are most often made. Fibroserous and suppurative pleurisy both occur in early life, but the purulent form is relatively more common in infancy and not infrequently occurs *d'emblée*. The prevalence of the purulent disease in infancy is shown by the modern records of the Hospital for Sick Children. Dr. Henry K. Dillard informed me once that when he was resident physician at the Children's Hospital in Philadelphia there were five infants, varying in age from ten months to two years, operated upon for empyema in one winter. The operation in each case was by free incision and resection of one rib. The patients all recovered. In the Children's House of the Bryn Mawr Hospital there were eleven patients, mostly infants, operated upon for empyema within one year. The physical signs of pleurisy in children often resemble those of pneumonia, and it requires great care on the part of the physician to avoid a diagnostic error. The chief source of confusion is the persistence of bronchial breathing throughout the dull region of a large effusion, with entire absence of vocal fremitus. In different parts of the affected side of the chest the respirations may be intensely tubular. Friction sounds are rarely heard in young children, and the same may be said of feebleness of the breath sounds. Another difference is the comparative absence of visceral displacement, which is accounted for by the flexible chest of the child yielding readily to fluid accumulation, pressure not being expended upon the adjacent organs to the same extent at least as in the adult.

The diagnosis of pleurisy is readily made in most instances. An uncomplicated and well-characterized case cannot be confounded with any other affection. That is, when distention of the chest, absolute dulness on percussion, faintness or absence of vocal fremitus, feebleness or absence of respiratory murmur, and displacement of viscera coincide with pain, irregular breathing, and fever. If the general symptoms be too much relied upon the diagnosis in many cases would be puzzling, but with the aid of the physical signs a satisfactory conclusion can be promptly reached. Pneumonia, with pleurisy is often confounded, but differs from the latter in the violence of its initial chill and the character of the pain, which in uncomplicated pneumonia is moderate and dull. The cough of pneumonia is deeper and the sputum viscid and rusty. The chest is not enlarged, the vocal fremitus is often intensified in the dull region, and the heart and liver are not displaced. The dulness on percussion is not absolute as it is in pleurisy, and the resistance to the finger in the latter is greater. The semitympanitic resonance on percussion in pleurisy with large effusion characteristically exists above the level of the fluid. In rare cases a tympanitic sound on percussion is perceived in pneumonia, but it is then most pronounced over the consolidated lung. In pneumonia loud bronchial respiration is heard over the whole of the consolidated portion of the lung, but in pleurisy with large effusion, excepting in infancy and childhood, a tubular quality of breathing is rarely heard below the level of the fluid. There may be bronchial respiration in the dull area when a slight pleuritic effusion exists, but it will not be accompanied with bronchophony but with egophony, a state of voice rendered bleating by the interposition of a layer of fluid between the costal and pulmonary pleura.

The presence of pus in the pleural cavity is to be suspected when the temperature rises and assumes a persistent remittent form, the patient at the same time often complaining of a sense of chilliness. An auscultatory sign of value is the non-transmission to the ear of the whispered voice through the fluid (Bacilli) sign ("pectoriloquie aphoniquë"). The only positive means of determining the character of the fluid is by exploratory puncture.

Hydrothorax is distinguished from pleurisy by the absence of fever in the former and by the fact that simple transudations are usually bilateral and are frequently associated with dropsy in other parts of the body. I have had the opportunity of observing three cases of unilateral serous transudation into the pleural cavity: one the result of circulatory pressure of a cancerous growth in the mediastinum and two from the pressure of enlarged bronchial glands in Hodgkin's disease.

Acute primary pleurisy in robust subjects usually ends in recovery without leaving serious after effects. But secondary pleurisies are always serious according to the gravity of the infection with which they are associated. In the treatment of the early stage, pain is much relieved by strapping the affected side of the chest or by the local application of a cold compress. When the patient dreads the cold, or if its application fails to keep the pain in check, hot flaxseed poultices, frequently changed may be substituted. An occasional hypodermic injection of morphin gives additional comfort. The patient should be kept absolutely quiet in bed on restricted diet, until the decline of the fever. Internal medication is indicated by special symptoms. Diaphoretics are sometimes useful for modifying the pyrexia in the early stage of the disease. After the decline of the fever, the effusion having apparently reached its maximum, and when scanty secretion of the kidneys is still an existing symptom, the exhibition of diuretics is called for to stimulate absorption of the fluid. The bowels should also be kept freely evacuated, administering, if required, saline laxatives occasionally preceded by calomel followed by a purgative. The operation of thoracentesis should be performed in all cases in which the pleural cavity is largely filled with fluid, and in others with excessive dyspnea or when signs of absorption fail to appear. The internal and external use of iodin and finally of muriated tincture of iron will hasten absorption of fluid and inflammatory thickening of the pleuræ.

Pus in the pleural cavity should be promptly removed by free incision and rib resection to establish free drainage. An unexpanded lung and consequent retraction of one side of the chest are subject to improvement or cure by pulmonary gymnastics and systemitized exercise of the body in general.

RECURRENT PNEUMOTHORAX: REPORT OF A CASE, WITH REVIEW OF THE LITERATURE.

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Medical literature is replete with studies of pneumothorax, and although cases of presumed spontaneous pneumothorax are not specially common, the subject has been well considered. In attempting to ascertain the frequency of recurrent pneumothorax we found that little had been written concerning it. In Albutt's *System*,[1] Finlay says that "as a curiosity attention may be directed to recurring pneumothorax: these cases are accompanied by few symptoms, nearly always recover, and may therefore be due to rupture of emphysematous bullæ." Neither in Osler's *Modern Medicine*[2] nor in Nothnagel's *Encyclopedia of Practical Medicine*[3] is even mention made of this phase of the subject under the general head of "pneumothorax."

In 1888 Gabb[4] reported a case which he had seen in one attack of pneumothorax. The patient, a female, had had three preceding attacks and had been under the care of Dr. Byrom Bramwell and his father. Her age at the time of the first attack, fourteen years previous, was forty-two. She had also had bronchitis and pleurisy of the right side in addition to the attacks of pneumothorax. In this case the pneumothorax had appeared on the same side each time. In the first attack air filled the entire right pleural cavity, but in the second the pneumothorax was localized and limited. Dr. Bramwell had been unable to find any evidence of tuberculosis, but stated that the family history was bad. One sister had a well-marked phthisis at the time of the patient's first pneumothorax. Byrom Bramwell advanced the theory that the first attack was due to the pulling upon an adhesion at the right apex during violent effort, so rupturing the lung. As the air was absorbed a friction rub appeared. Three of the attacks were on the same side. The location of one is not stated.

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[1] Albutt and Rolleston, 1909, v, 575.

[2] Walter R. James, iii, 868.

[3] O. Rosenbach, Pneumothorax, p. 972.

[4] Recurrent Pneumothorax, British Med. Jour., 1888, ii, 178.

In 1892 Vitvitski[5] saw a young man, tailor by occupation, who complained of shortness of breath, cough, and general weakness. The family history was unimportant, except that his father died at the age of forty years of tuberculosis. A year preceding this illness the patient had noted cough and pain in the chest. His pains were temporary at first, but his health soon became so much impaired that he had to give up his occupation. At one time there appeared very suddenly dyspnea, with considerable pain in the left chest. This shortness of breath, however, passed in a few days. Two months previous to his admission to the hospital he began to have diarrhea and vomiting after taking food. Physical examination showed that he had a left-sided pneumothorax with cavity formation on the right side, well-marked signs of general pulmonary tuberculosis, and tuberculosis of the kidney. He died eight days after admission to the hospital, and the clinical findings were confirmed by the autopsy. Examination of the left chest showed not only a pneumothorax but a scar in the pleura, the size of a lentil evidently the location of the perforation of the preceding pneumothorax.

In 1898 Finny[6] recounted the history of a young man whom he had observed in two different attacks. His age at the time of his first admission to the hospital in 1897 was eighteen. The pneumothorax was on the left side. He was discharged from the hospital about five weeks later. During the absorption of air, dry pleurisy appeared. Two weeks after his discharge he reappeared at the hospital, with return of the signs and symptoms on the same side. There is no record of subsequent observation. It is of interest to note that no family history of tuberculosis was obtained.

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[5] A Case of Recurring Unilateral Pneumothorax, Vrach, St. Petersburg, 1894, xv, 960.

[6] Dublin Jour. Med. Sci., 1898, cv, 273.

In 1907 Sale[7] reported a remarkable case which had come under his observation. The patient, a young woman, aged twenty-two years, had had eleven attacks of pneumothorax. In her case there was no history of familial tuberculosis. The first attack was preceded by a period of coughing and spitting of blood. There had been no fluid in the chest at any time. He did not consider that a tuberculosis infection was the causative factor.

In 1908 Hamilton[8] reported the subsequent course of 4 cases of pneumothorax whose histories had been given in a previous article. One of these cases had two attacks of pneumothorax, both on the right side. Ten years after the last attack the patient was in good health and had had no recurrence of the condition. There was nothing in this case which Hamilton considered indicative of a tubercle infection. He was under observation eleven years.

The following case came under my observation: J. H., unmarried male, aged twenty-three years. To my personal knowledge he had been in excellent health since childhood. In the family history the only significant point was the fact that his only brother had suffered at one time, some years previously, from a tuberculous elbow. This had healed after immobilization. His father and only sister were in good health. His mother died of cardiac disease. He walked to my residence on February 13, 1912, complaining of severe pain in the right side. It appeared suddenly the same day while taking his morning bath. He had been in the enjoyment of his usual good health. Temperature 98° F., pulse 80, respiration 20. There was no evident dyspnea. Physical examination at once showed that the left side of the chest was distinctly more voluminous than the right. The supraclavicular space and the intercostal spaces on this side were filled out and the intercostal depressions were not visible. Respiratory movement was slight on both sides. On the affected side, tactile fremitus was absent, while the breath sounds were distant, high-pitched, of metallic quality, with inspiration and expiration of about equal duration and intensity. The heart was pushed over to the right, the right border of dulness being 5 cm. to the right of the midsternal line and the left border being 8 cm. to the left of the same line in the fifth interspace. The point of maximum cardiac impulse was in the sixth interspace, 4 cm. to the left of the midsternal line.

Aside from the pain in the chest the patient felt perfectly well and wanted to be out. He did not seem to be ill. He was sent home and kept at rest, but would not remain in bed. February 15 his general condition remained excellent. The white blood cells were 12,000 per c.mm. Examination of the chest showed that the left side was full and immobile. The lower border of the resonance was in the ninth interspace in the axillary line and in the eleventh interspace in the scapular line. I was unable to demonstrate the coin sound.

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[7] Lancet, 1907, ii, 1572.

[8] Spontaneous Pneumothorax, Montreal Med. Jour., 1908, xxxvii, 492.

On February 18 the patient developed a complicating follicular tonsillitis, in consequence of which the temperature rose to 101.4°. The chest showed decided change. Pulmonary resonance was demonstrated at the usual points. The heart had resumed practically its normal position. The breath sounds were fairly well heard over the entire left chest except at the base posteriorly. A distinct friction rub was heard in the lower portion of the axilla and below the heart when the patient was in the reclining posture. On February 21 (eight days after onset) the physical signs had largely disappeared. The friction rub in the axilla was less and the breath sounds were not so distinct. The patient resumed his usual duties as a surveyor in about three weeks after the onset of the pneumothorax. Frequent examinations failed to show any deviation from normal.

July 13, 1913, the patient consulted me again, complaining as before of pain in the chest. This had come on suddenly. The left chest looked much fuller than the right, but it moved well on respiration, and this time the heart was not displaced. Over the entire left chest the percussion note was slightly tympanitic except at the left base posteriorly, where it was dull. Over the entire left chest the breath sounds were very distant, except over the base posteriorly, where they were absent. Tacticle fremitus was lessened throughout; over the base it was absent. No adventitious sounds were heard.

July 19 the patient reported that the pain was less. The physical findings, however, were about the same.

July 24, Drs. W. C. Hill and G. F. Thomas made stereoscopic Roentgen-ray plates. They showed a pneumothorax on the left side with what was evidently a band of adhesions running between the right pleura and the pericardium. Shadows seen in the right chest were considered by Drs. Hill and Thomas to be caused by foci of healed tuberculosis. The patient was then reëxamined very carefully. On percussion the note over the apex of the right lung proved to be slightly shorter in duration and higher in pitch than normal. An expansion of 1.5 cm. was present at the apex. The breath sounds were normal except for slightly high pitch. Vocal and tacticle fremitus were normal throughout the right lung. No rales were heard anywhere.

August 7, the twenty-fifth day after onset, the patient reported that he suffered practically no pain. Physical examination showed that the signs of pneumothorax had practically cleared up. Resonance was the same on both sides and breath sounds were transmitted as well on one side as the other, with the exception that over the right apex posteriorly, resonance was somewhat deadened. On expansion the right apex did not move as freely as the left. Since this time the patient has been examined frequently.

July 23, 1914, no deviation from normal could be detected anywhere. His weight is and has been for some months at his normal maximum. He feels perfectly well, looks well, and is engaged daily in his occupation.

August 18, 1914, Drs. Hill and Thomas again made a Roentgen-ray picture, which showed normal relations between pleura and lungs. The amount of presumed tuberculous involvement was the same as in the previous finding.

In discussing this history my own conclusion is that a dormant tubercle infection explains the etiology. In favor of this view we have Roentgen-ray plates demonstrating the existence of apparently healed foci and the presence of slight though definite physical signs at one apex, together with a transitory, dry pleurisy. The band of adhesion running between the right pleura and the pericardium, as reported by the roentgenologist, is extremely interesting in connection with the theory advanced by Byrom Bramwell in one case (Gabb).[9] One is forced to admit that the continued good health of the patient weighs heavily against this theory. It is quite possible, however, that the pneumothorax has served in this case, and perhaps in all the other reported cases but one, as a therapeutic measure, and that its occurrence has tended to retard the flaring up of a slight tuberculous focus.

In analyzing the reports, which comprise all that I have been able to discover in the literature, we see that the accompanying history gives a total of six cases. Of this number four had only two attacks (Vitvitski,[10]; Finny,[11] Hamilton[12]), but of the three one was observed but a short time and one died. One case (Gabb)[13] had four attacks and one had eleven. In some instances only a few months elapsed between the disappearance of air in the pleural sac and its reappearance, while occasionally one or two years intervened.

It is of interest to note that in one case the time elapsing between the first attack and the fourth was fourteen years, and that Sale's[14] case had all of her eleven attacks in six years.

We can find no positive evidence that more than one side was affected in any instance. It is stated by Gabb[15] that the right side was the seat of the trouble three times. The location of one seizure is not noted. Finny,[16] Vitvitski,[17] and Hamilton[18] specify that the trouble made its second appearance on the same side. Sale[19] states that three attacks were on the right side, but fails to note the location of eight. The fact must have some significance in considering the pathology, and does not bear out the theory advanced by certain writers that so-called idiopathic pneumothorax is due to the rupture of emphysematous vesicles. If this were true the condition would be expected to affect the two sides impartially.

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[9] Loc. cit.
[10] Loc. cit.
[11] Loc. cit.
[12] Loc. cit.
[13] Loc. cit.
[14] Loc. cit.
[15] Loc. cit.
[16] Loc. cit.
[17] Loc. cit.
[18] Loc. cit.
[19] Loc. cit.

One case only, the one which terminated fatally, presented undeniable signs of infection with tubercle. Another had a family history of tuberculosis, and had had bronchitis and pleurisy in the interval between two manifestations of pneumothorax. A third case gave a history of cough and bloody expectoration preceding her first pneumothorax. One case showed Roentgen-ray findings pointing to tubercle infection. In the remaining two cases there was no apparent valid reason for suspecting the presence of a latent tuberculosis.

Conclusions regarding the etiology of recurrent pneumothorax would be out of place with so little data at hand. It is reasonable to suppose that it is the same as in cases of "spontaneous" pneumothorax. The etiology of this condition has been quite thoroughly discussed, West[20] making the point that tuberculosis is always the causative factor. This series of cases, with four showing definite or suggestive signs of tubercle infection, is not without interest.

A CLASSIFICATION AND ANALYSIS OF CLINICAL TYPES OF SPLENOMEGALY ACCOMPANIED BY ANEMIA.[1]

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Chronic splenomegaly, usually associated with anemia, is not an uncommon condition both in adults and children. The forms without leukocytosis, more or less related to "splenic anemia," it is my intention to consider here, omitting the types of enlarged spleen in which other features render differentiation easy (such as leukemia, pseudoleukemia, polycythemia, and those secondary to obstruction or infection, as in heart disease, typhoid, kala-azar, syphilis, and so forth).

Splenic Anemia. The connection between chronic enlargement of the spleen and marked anemia without leukocytosis, as denoted in the term "splenic anemia," was first established forty-eight years ago by Gretzel,[2] in Griesinger's clinic, in Berlin. He described the case of a child, ten months old, suffering from dysentery and severe anemia, with considerable enlargement of the spleen and lesser enlargement of the liver and lymph nodes. Examination of the blood showed that the proportion of white to red cells was not increased—that is, that it was not leukemia. Five years later H. C. Wood[3] described a "splenic variety" of pseudoleukemia, with a report of a case with a greatly enlarged spleen, severe anemia, and without leukocytosis. It must be remembered that at this time not only was pathological anatomy in its infancy, but also no exact methods existed for examining the condition of the blood. A term, therefore, like "splenic anemia," which a half century ago was a distinct advance in differentiating a new type of disease, but which now is known to include several distinct types, should now either be properly restricted or discarded entirely. By restriction I mean limitation of the term to the earlier or precirrhotic stages of Banti's disease, with which it is apparently identical. The fact that in most cases the etiology or pathogenesis of this group of diseases is not yet clearly understood is no more an argument for continuing to group them under such loose terms as "splenic anemia" or "splenomegaly with anemia" than it would have been to group typhoid with typhus fever until the discovery of the Bacillus typhosus. Though much still remains to be learned in regard to them, and though probably even their present eponymic or cumbersome names are only temporary, nevertheless it has already become more profitable to deal with them as independent affections. The inconvenience resulting from the present use of the term "splenic anemia" is quickly demonstrated to anyone making a critical survey of the literature. Statistical summaries, including valuable detailed information, are thus frequently rendered useless when, on analysis, they are found to include several independent types.

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[20] Samuel West, Pneumothorax, Lancet, 1897, i, 1264.

[1] Being part of an address read before the Joint Meeting of the Pediatric Societies, New York Academy of Medicine, November 5, 1914.

[2] Ein Fall von Anemia Splenica bei Einem Kind, Berl. klin. Woch., 1866, ii, 212.

Recently evidence has been put forth to show that these conditions are perhaps related to other commoner diseases, such as pernicious anemia, various hemolytic anemias (Dibothriocephalus latus and uncinariasis), thrombosis of the portal vein or artery, and some splenic types of cirrhosis of the liver. It will be beyond my scope to more than indicate such relations. The better differentiated of these offsprings of splenic anemia are Banti's disease, Gaucher's disease (or large-celled splenomegaly), v. Jaksch's pseudoleukemia infantum, the Hayem-Widal or acquired form of hemolytic jaundice with splenomegaly, and the Chauffard-Minkowski or congenital or hereditary form of the same. I have indicated some of the differential points of these diseases in the following table:

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[3] On the Relation of Leukocythemia and Pseudoleukemia, Amer. Jour. Med. Sci., 1871, lxii, 373.

TABLE I.—DIFFERENTIAL DIAGNOSIS.

	Etiology.	Pathology of spleen.	Family history.	Time of onset.	Duration.	Icterus.	Splenomegaly.	Hemorrhages.	Anemia	Resistance of red blood cells.	Reticulated red blood cells.	Uro-bilinuria.	Leukocytes in blood.	Liver.	Treatment.
Gaucher's disease	Toxin ? Infection ? Tumor?	Peculiar cell hyperplasia	Occasionally positive	Childhood	Many years	Rare	+++	Occasionally	Slight	?	?	?	−	+	Splenectomy ?
Banti's disease	Toxin ? Infection ?	Hyperplasia fibrosis	Negative	Adult life	Few years	Rare	+	Occasionally	Slight to severe	Normal	Normal	+	−	First + Later −	Splenectomy.
v. Jaksch's disease	Rachitis ?	Hyperplasia fibrosis	Negative	Infancy	Several months	Rare	++	?	Slight to severe	?	?	?	+	+	Splenectomy ? Iron, arsenic, etc.
Hayem-Widal	1. Primary ? 2. Secondary to infection	Congestion and pigmentation	Negative	Any age	Many years	Present	++	Rare	Severe	Diminished	Increased	+	−	+ or normal	Splenectomy.
Chauffard-Minkowski	Heredity	Congestion and pigmentation	Positive	Congenital or childhood	Many years	Present	++	0	Slight	Diminished	Increased	+	−	+	Splenectomy.
Pernicious anemia	Enterogenous toxin ?	Fibrosis	Negative	Adult life	Few years with remissions	Very rare	Slight or diminished	Rare	Severe	Increased	Increased	+	− or +	Normal	Iron, arsenic, etc. (splenectomy questionable).

Gaucher's Disease. Gaucher's disease, or large-celled splenomegaly, was probably the first variety to be differentiated on account of its peculiar anatomical picture. Although in reality possessing little in common with the other forms of splenic anemia, I will consider it in some detail on account of the similarity of the clinical picture and from the fact that it is still included by many writers under this heading. First described by Gaucher,[4] in 1882, as a primitive epithelioma it was later shown not to possess the characters of malignancy. Bovaird[5] called it a simple hyperplasia and Brill and Mandlebaum[6] showed that it arose simultaneously from the endothelium of the spleen, lymph nodes, and bone-marrow. The characteristic large vesicular cells, with small eccentric nuclei, blocking the sinuses of the spleen and lymph nodes or crowded in the capsules of the liver lobules should make the diagnosis easy at autopsy. Careful analysis by the last-named authors, however, with rejection of falsely diagnosed cases, has reduced the number of reported cases to fourteen. Since that time five apparently true cases have been reported by Knox and Wahl[7] and Hermann.[8] Brill and Mandlebaum's excellent summary reveals the following clinical picture: The disease begins insidiously in infancy or childhood (usually before the thirteenth year) and pursues a chronic course (average of twenty years). As in some of the other varieties a history of similar trouble in the family is frequently elicited. No great disturbance in the health of the individual occurs until the disease has persisted for some time, when distinct anemia appears and, as in Banti's disease, a definite tendency to submucous or subcuticular hemorrhages. These, however, are never fatal, and death usually occurs from an intercurrent affection. The most prominent symptom is the progressive enlargement of the spleen, which may reach greater proportions than in any other disease, eventually filling most of the abdomen. The abdominal discomfort produced by the enlarged spleen may be the first indication of the disease. As in Banti's disease the blood changes are not very characteristic. The anemia of chlorotic type is never very severe (average red blood corpuscles count of advanced cases being 3,700,000). A definite leukopenia is usually found, though the differential count remains unchanged. No enlargement of the superficial lymph nodes can be found, and jaundice and ascites are rarely present. Liver enlargement, succeeding that of the spleen, may eventually reach considerable proportions.

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[4] De l'Epithelioma Primitif de la Rate, Thèse de Paris, 1882.

[5] Primary Splenomegaly, Endothelial Hyperplasia of the Spleen, Amer. Jour. Med. Sci., 1900, cxx, 377.

[6] Large-cell Splenomegaly (Gaucher's Disease), Amer. Jour. Med. Sci., 1913, cxlvi, 863.

[7] A Case of Primary Splenomegaly of the Gaucher Type, Med. Rec., 1914, lxxxvi, 606.

[8] A Case of Gaucher's Disease, Med. Rec., 1914, lxxxvi, 606.

A brownish discoloration of the skin has been noticed with a "peculiar yellowish wedge-shaped thickening of the conjunctivæ, commonly seen on both sides of the corneæ." In spite of the rather negative character of the symptoms the disease has been recognized three times during life, with confirmation of the diagnosis by histological examination.[9]

Its etiology is still in doubt. Malignancy having been discarded, various theories of endogenous toxins, splenic enzymes, or of infection have been offered, but supported by very little evidence.

In regard to the bearing of experimental spleen work on this disease, but few facts exist to help us. Splenectomy has been tried in nine cases, with three deaths. This probably represents too high a mortality, but, on the other hand, a cure could hardly be expected, as the disease is known to exist independently in bone marrow and lymph nodes. The resistance of the red cells and number of skeined cells (as evidence of blood regeneration), as far as I can find, has not been studied, but in view of the absence of signs of increased hemolysis, one would not expect to find any noteworthy changes in such examinations. The red bone marrow, usually found at autopsy, on the other hand, would point to efforts at regeneration. As the splenic tissue is largely replaced by the peculiar Gaucher type of cell, it may be that this stimulated marrow is equivalent to that found experimentally after splenectomy.

Summing up: this disease, in spite of being frequently included among other forms of splenic anemia, has but little in common with them clinically, beyond the chronically enlarged spleen and anemia. Pathological examination should always admit its proper diagnosis to be made.

In the past few months, under the title of "an unknown disease picture," Niemann[10] has described a form much resembling Gaucher's disease, but running an acute course, with fatal termination after fifteen months. The finding of similar large endothelial-like cells at autopsy make it probable that an acute form of this disease must also be recognized.

Banti's Disease. For the more common condition of Banti's disease, or splenomegaly with hepatic cirrhosis, a brief summary will suffice to recall its general symptomatology. First described by Guido Banti[11] in 1894 the clinical picture presented at that time still holds. Usually occurring in young otherwise healthy adults, and running a chronic course, its symptomatology may be divided into three periods: in the first or pre-ascitic period, usually lasting several years, a gradually increasing weakness and pallor are noticed with digestive disturbances and abdominal pain, which may first call attention to the enlarged, smooth, hard spleen. A tendency to hemorrhages with a moderate anemia of chlorotic type is usually present, but may be postponed until the later stages. There is nothing specially characteristic in the anemia, the increase of urobilin being the only sign of increased blood destruction. The resistance of the red cells is unchanged; signs of a regenerating bone marrow (nucleated and reticulated red cells) are slight or absent. After splenectomy, however, such changes may be noted. In such a case that I have recently had occasion to examine the red cells showed the most marked increase in resistance that I have seen clinically (complete hemolysis did not occur even at 0.25 per cent. NaCl). Though no nucleated reds were present in the circulation, reticulated forms were more numerous than before splenectomy. A slight leukopenia is characteristic. The second, or intermediate, stage lasts but a few months, is characterized by scanty, high-colored urine, containing an excess of urobilin; and by attacks of dyspepsia and diarrhea, with slight increase in the size of the liver. The third stage is ushered in by the symptoms of cirrhosis, a recurrent, painless ascites, occasionally slight jaundice, shrunken liver, and increasing anemia and emaciation. After a few years an intercurrent infection or fatal hemorrhage terminates the scene. The first two of these periods are identical with the "splenic anemia" of adults. It is hardly necessary to say that such a picture is subject to variation, and that in some cases these three periods cannot be distinguished.

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[9] While this paper was in press, Bernstein has reported (Jour. Am. Med. Assoc., 1915, lxiv, 1907) a fourth case diagnosed by clinical symptoms, and confirmed before operation by splenic puncture.

[10] Ein unbekanntes Krankheitsbild, Jahrb. f. Kinderheilk., 1914, lxxix, 1.

[11] La Splenomegalia con Cirrosi Epatica, Lo Sperimentale, 1894, Sez. Biol., xlviii, 407.

In spite of the great amount of work done on Banti's disease in the past twenty years its pathogenesis is still undetermined. Except for a recent statement by Gibson[12] that he had found streptothrix in certain cases of enlarged spleen resembling Banti's disease, its etiology is still unknown. Yates, Bunting, and Kristjanson[13] have found diphtheroid organisms in several cases of Banti's disease, and consider the condition closely related to that of Hodgkin's disease. An apparently identical syndrome can be brought about by thrombosis of the portal or splenic vein (Edens,[14] Goldmann[15]), and similar clinical pictures have followed various infections, local trauma, etc. Hollins[16] has recently produced a similar condition in rabbits with injections of Bacillus coli. Banti, who first considered the enlargement of the spleen to be primary, later stated that the infectious agent was brought by the artery either as a direct toxin or as a substance which, from the pathological splenic metabolism, was changed into a splenotoxin. The theory has never been confirmed by facts. The unquestioned improvement, however, that results in many cases after splenectomy, proves that the altered spleen is at least an important pathogenetic factor. This is still further emphasized by Umber's[17] interesting observation: during splenectomy for Banti's disease in a boy, aged fifteen years, a small piece of the enlarged liver was excised for histological examination and a distinct peripheral infiltration found. After the operation the liver quickly returned to normal size, a strong indication of the splenogenous origin of the hepatitis which, if undisturbed, would have progressed to the usual cirrhosis. In metabolic experiments on this patient, Umber found a nitrogen deficit that was changed to a nitrogen balance by splenectomy. This, however, has not been confirmed by later authorities.

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[12] On Certain Causes of Splenomegaly and Banti's Disease, Proc. Roy. Soc., 1914, vii, Med. Sect., 7.

[13] The Etiology of Splenic Anemia or Banti's Disease, Jour. Amer. Med. Assoc., 1914, lxiii, 2225.

[14] Ueber Milzvenenthrombose, Pfortaderthrombose und Bantische Krankheit., Mitth. a. d. Grenzg. d. Med. u. Chir., 1907, xvii, 59.

[15] Zur Kasuistik der Milzvenen u. Pfortaderthrombose, Deut. med. Woch., 1913, xxxix, 1542.

[16] Primary Splenomegaly or Splenic Anemia, Practitioner, 1915, xciv, 426.

In the pathology of the disease there is nothing specially distinctive. The enlarged spleen usually shows an increased amount of fibrous tissue in the capsule and reticulum known as "fibro-adenie" (that is, increased fibrous tissue, but retaining an adenoid appearance), and involving both pulp and follicles. The Malpighian follicles, especially in the later stages, are small and scarce; in the earlier stages they may be hyperplastic and the "fibro-adenie" be absent. Macrophages, increased amount of pigment, and other evidences of increased blood destruction are usually found. The changes in the liver are those of an ordinary periportal cirrhosis.

In summarizing, one might say that although the etiology of Banti's disease is unknown, and may well be from several sources, evidence points to the close causative relationship of the spleen. One would not expect the removal of the largely fibrotic organ of the later stages to be attended with marked somatic changes, and it is precisely in the earlier stages of the disease in which splenectomy has proved most beneficial.

Von Jaksch's Disease. The anemia infantum pseudoleukemica of von Jaksch is in all probability not an independent condition, but represents an atypical response of the infantile hemopoietic system to one of the primary diseases of the blood (leukemia, pernicious anemia, the secondary anemia of rickets, syphilis, or the formerly unrecognized types of hemolytic jaundice). A high-grade anemia, with blood picture somewhat resembling pernicious anemia, appears in infants of one or two years. The smooth, hard spleen is conspicuously large, while the liver, in contrast to the liver of leukemia in childhood, is slightly enlarged. Benjamin has lately found rickets present in all of a series of such cases examined by him, and suggests the name "Rachitische Megalosplenie." That von Jaksch's disease is being less and less regarded as a separate disease is shown by its gradual disappearance from the text-books.

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[17] Zur Pathologie der Bantischen Milz Krankheit, Münch. med. Woch., 1912, lix, 1473.

HEMOLYTIC JAUNDICE. The acquired and congenital or familial types of hemolytic jaundice with splenomegaly (Hayem-Widal and Chauffard-Minkowski) are frequently grouped by English and American authors under such titles as hemolytic jaundice (Thayer),[18] chronic family jaundice (Tileston).[19] As the two forms possess several rather important and characteristic differences, however, I have deemed it advisable to follow the continental custom and consider them as independent conditions. Search for their true etiology and pathogenesis is more apt to be stimulated under such an arrangement than if they are grouped together. Furthermore, Widal, Abrami and Brulé,[20] experimenting with toluylendiamin, have offered evidence that the two types are of different origin.

They have been so recently differentiated that they can be best considered together in their historical development. Although Murchison,[21] Wilson,[22] and others had previously described cases of chronic jaundice occurring in several members of a family (in Murchison's case splenomegaly is not mentioned), a more complete description by Hayem,[23] in 1898, was the first to establish an independent clinical condition. The clinical picture of the five cases analyzed by him was as follows: All five exhibited a chronic jaundice, with the presence of bile pigment in the blood serum, but not in the urine (*i. e.*, acholuric icterus). The other signs of obstructive jaundice, such as itching, bradycardia, and clay-colored stools, were also lacking. A distinct anemia, the red-cell count varying from 1,000,000 to 3,000,000, was present in all. Very large, hard spleens were found in each case and slight enlargement of the liver was also noted. Exacerbations were frequent, in which the jaundice deepened and bile appeared in the urine. The importance of these exacerbations was emphasized by Widal, who termed them "crises of deglobulization," and considered them highly characteristic of the acquired form. In severe cases the blood count may drop below 1,000,000, and hemoglobin appear in the urine. In all five of Hayem's cases the family history was negative, and in three the jaundice was stated to have appeared first in adult life.

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[18] Hemolytic Jaundice, Illinois Med. Jour., 1911, xix, 174.

[19] Chronic Family Jaundice, AMER. JOUR. MED. SCI., 1910, cxxxix, 817.

[20] Pluralité d'Origine des Ictères Hemolytiques, Bull. et Mém. Soc. Méd. des Hôp. de Paris, 1907, xxiv, 1354.

[21] Case of Hereditary Jaundice and Gout, "Diseases of Liver," 1885, p. 481 (3d ed.).

[22] Some Cases Showing Hereditary Enlargement of the Spleen, Trans. Clin. Soc., London, 1890, xxiii, 162; ibid., 1893, xxvi, 163.

[23] Sur un Variété Particulière d'Ictère Chronique, Ictère Infectieux Chronique Splenomegalique, Presse Méd., 1898, i, 121; Nouvelle Contribution à l'Etude de l'Ictère Infectieux Chronique Splenomegalique, Bull. et Mém. Soc. Méd. des Hôp. de Paris, 1908, xxv, 122.

Two years later Minkowski[24] described a similar disease occurring in eight members of one family in three generations. This has subsequently proved to be commoner than the acquired form. In addition to the symptoms of Hayem's cases an increased amount of urobilin was noted in the urine. Autopsy revealed no cirrhosis of the liver or obstruction of the bile passages. The spleen showed a diffuse hyperplasia and hyperemia. Pigment deposits were numerous in the kidneys and centres of the liver lobules.

The next important contribution to the clinical picture of these diseases was made by Chauffard,[25] who showed in the congenital type that the resistance of the red-blood cells to hypotonic salt solution was much diminished. This simple test, suggested in 1903 by Ribierre,[26] has proved so useful in our experimental work that I take the liberty of describing it briefly:

A series of twelve or more tubes containing 1 c.c. of different strengths of hypotonic salt solution are arranged varying from 0.25 per cent. to 0.6 per cent. (or even stronger if diminished resistance is suspected). Into each one drop of whole blood is introduced and the tube gently shaken. If the drops have been of different size, occasionally slightly more blood may be added until the color is the same in all. After standing two hours at room temperature, in the stronger solutions in which no hemolysis has occurred, the unchanged corpuscles at the bottom of the tube will be overlaid with colorless salt solution. In the weakest solutions all corpuscles will have been hemolyzed, forming a transparent red solution. In the intermediate tubes can be noted at which strength hemolysis begins and at which it is complete. In normal cases, hemolysis begins at about 0.45 per cent. and is complete at 0.35 per cent. In a case of the familial type that I recently had occasion to examine, hemolysis began as high as 0.7 per cent. and was already complete at 0.475 per cent. Widal, Abrami and Brulé showed that in some cases of the acquired form, with apparently normal resistance, fragility could be demonstrated if the cells were washed free of plasma. Later work, however, has shown that any change, when present, is in the cells themselves.

Increased number of microcytes and of reticulated red cells by methods of vital staining were found by Chauffard[27] in the congenital, or familial type, and their presence later confirmed also in the acquired type. In the case above mentioned I found about 5 per cent. of the red cells reticulated as opposed to the normal of less than 1 per cent. In some cases the figures have run as high as 20 per cent. Although Chauffard used pyroninmethyl green stain and Widal, polychrome methylene blue, we have obtained the best results with brilliant cresyl blue. A few drops of blood are dropped into a small test-tube containing a weak solution of the stain, with a little potassium oxalate to prevent rouleaux formation. After standing ten to fifteen minutes some of the sediment is pipetted off and a fresh cover-slip preparation made. The percentage of the reticulated to the non-reticulated forms is then estimated under oil immersion. If the reticulated cells are increased it is generally considered evidence of more active blood formation.

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[24] Ueber einem Hereditärischen unter dem Bild eines Chronischen Ikterus mit Urobilinurie, Splenomegalie und Nieren Siderosis verlaufende Affecktion, Verh. der Deut. Kong. f. inn. Med., 1900, xviii, 316.

[25] Pathogenie de l'Ictère Congenitale de l'adult, Semaine Méd., 1907, xxvii, 25; Les Ictères Hemolytiques, Semaine Méd., 1908, xxviii, 49; Pathogenie de l'Ictère Hemolytique Congenitale, Annales de Méd., 1914, i, 1.

[26] L'Hemolyse et la Mesure de la Resistance Globulaire, Thèse de Paris, 1903.

[27] Loc. cit.

Another diagnostic method, the auto-agglutination test, is advocated by Widal, Abrami and Brulé.[28] This test consists merely of mixing one drop of the patient's washed red blood cells with ten drops of his own serum in a watch-glass. If positive, after some seconds, the mixture loses its homogeneous aspect, forms visible granules of agglomerated corpuscles on agitating, and finally, after several minutes, forms a distinct pellicle that sinks to the bottom and does not mix with the clear serum on shaking. They have found it always positive in the acquired form and always negative in the congenital or familial type. In the case I have previously mentioned this test proved negative. However, in Micheli's[29] carefully studied case of the acquired type this test was also negative. Isohemolysins have occasionally been found in both types (Micheli;[30] Hopkins[31]) but are not supposed to possess any pathological significance. Although both types of hemolytic jaundice usually run a chronic course, Gaisböck[32] has shown that an acute malignant form may occur that is fatal in a few months.

Therefore, the cardinal symptoms of these types of hemolytic jaundice with splenomegaly are found to be a chronic enlargement of the spleen, existing with an acholuric, non-obstructive jaundice, and anemia, frequently paroxysmal in character and varying in intensity. Increased blood destruction is indicated by increased urobilin in the urine, and various characteristic changes are found in the blood. The red cells show diminished resistance to hypotonic salt solution, increased number of reticulated cells with vital staining, and in the acquired form the phenomenon of auto-agglutination of the red corpuscles. The blood serum rarely contains auto- or isohemolysins.

[28] Auto-agglutination des Hematies, dans l'Ictère Hemolytique Acquis, Comp. Rendu. Soc. de Biol., 1908, lxiv, 655; Les Ictères d'Origine Hemolytique, Arch. des Mal. de Cœur, 1908, i, 193.

[29] Unmittelbare Effekte der Splenektomie bei einer Fall von Erworbenem Hemolytischen Splenomegalischen Ikterus, Wien. klin. Woch., 1911, xxiv, 1269.

[30] Loc. cit.

[31] Two Instances of Chronic Family Jaundice, Amer. Jour. Med. Sci., 1913, cxlvi, 726.

[32] Beiträge zur Klinik hemolytischer Anämien mit herabgesetzter osmotischer Erythrocyten Resistenz, Deut. Arch. f. klin. Med., 1913, cx, 413.

I have purposely postponed until now a consideration of the differentiation of the acquired and familial types and their relation to other conditions, such as those suggested by Gilbert[33] and Banti.[34] The fact that in the acquired group the disease is definitely acquired in adult life, whereas in the other there is a family history of the same trouble would not in itself be sufficient to warrant the formation of independent disease pictures. There are, however, other features which tend to differentiate their appearance more strongly. In the congenital form the subjects, as Chauffard puts it, "are more icteric than sick." Frequently they come for treatment for other conditions and consider the chronic jaundice as a family idiosyncrasy not interfering with perfect health. The acquired form, on the other hand, is usually ushered in with a definite attack of illness, the anemia becomes much more grave, sometimes as low as 1,000,000, and the patient is distinctly more anemic than jaundiced. In De Castello's[35] case, that showed great improvement after splenectomy, the red-cell count had previously fallen to 800,000.

In an analysis of 158 cases of hemolytic jaundice in which blood counts were available, I found 55 belonging to the acquired type and 103 to the congenital or familial type. Of these 103 only 23 failed to give a positive family history, whereas of the 80 familial cases 35 developed after birth. The average red-cell count of the 55 acquired cases was 2,032,000, the counts ranging from 510,000 to 4,500,000. (Counts below 1,000,000 were recorded in 10 cases, below 2,000,000 in 27 cases, and over 4,000,000 in only 4 cases.) The average count of the 103, congenital and familial, was 3,340,000, the counts ranging from 1,800,000 to 5,700,000. (N. B.—One familial case reported by v. Krannhals[36] showed 1,000,000 red cells in a single count, but as the hemoglobin was between 55 and 65 per cent. the accuracy of the count is questionable. No counts were recorded below 1,000,000, 8 below 2,000,000, and 25 above 4,000,000. The average of the familial cases was 3,281,000; of the congenital, 3,543,000.) These figures show that there is a much more marked anemia in the cases of the acquired type than in the familial.

Widal and his pupils claim that the auto-agglutination test is only positive in the acquired form, and considers it important evidence that the two diseases have fundamentally different origins. I have already called attention to the differential importance of

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[33] Cholémie Familiale, Bull. Mém. Soc. Méd. des Hôp. de Paris, 1907, xxiv, 1203. (N. B.—This contains references to all of Gilbert's work on this subject to date.)

[34] La Splenomegalia Emolitica, Patologica, 1911, iii, 471; La Splenomegalia Emolitica Anemopoietica, Sperimentale, 1913, lxvii, 323.

[35] Discussion of Kahn's case, Verhand. d. deut. Kong. f. inn. Med. (Wiesbaden), 1913, xxx, 331.

[36] Ueber Congenitale Ikterus mit Kronischem Milztumor, Deut. Arch. f. klin. Med., 1904, lxxxi, 596.

Widal's "crises of deglobulization," although it must be admitted that marked fluctuations are present also in the familial type.

Cases have been reported where a condition apparently identical with the acquired form under discussion has followed attacks of malaria, syphilis, and other infections, and further study will probably reveal that all cases of this type are due to more or less obscure intoxication. The signs of excessive blood destruction usually disappear from these cases when the underlying cause is successfully treated. The familial form, on the other hand, appears more as an inherited dystrophy of the hemopoietic system, rendering the red-blood cells more easily destructible. On this basis Chauffard at first strongly advised against splenectomy in this type, but subsequent cases have shown such improvement after this treatment that it would seem as if the removal of this site of blood destruction was advisable, whether or not it is the primary seat of the trouble. After Kahn's[37] and Roth's[38] successful splenectomies of the familial type the resistance of the red cells failed to return to normal.

The congenital type, with negative family history, grouped with the familial type by most authors, has less grounds for differentiation from the acquired form. The mere fact that the disease has already made its appearance at birth is of itself not of fundamental importance if there is no history of similar trouble in the family. I feel, therefore, that if the familial form (which, as a matter of fact, is usually, though not always, congenital) were opposed to the acquired form, the time of onset, as indicated by the term congenital, might well be disregarded. The possibility of an early acquisition of the disease is shown in the case reported by Beneck and Sabrazés.[39] With a negative family history, a suckling acquired the disease apparently from her wet-nurse, who, together with her two children, had a chronic hemolytic jaundice. Certain authors consider the two types identical. Hynek,[40] for instance, bases his opinion on two cases observed by him, the mother acquiring the disease after childbirth, whereas with her child it appeared congenitally. Plehn[41] reports a case appearing congenitally in father and daughter, but not until the twenty-sixth year in the case of a son. Benjamin and Sluka[42] observed three cases in one family, two appearing congenitally and one in adult life. Many of these could undoubtedly be harmonized if the time of onset was disregarded.

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[37] Ueber Hemolytischer Icterus und Seine Behendlung durch Splenectomie, Verh. d. deut. Kong. f. inn. Med., 1913, xxx, 326.

[38] Ueber die Hemolytische Anämie, Deut. Arch. klin. Med., 1912, cvi, 138; Der Angeborene Hemolytische Ikterus, Corresp. Schweiz. Aerzt., 1913, xliii, 689.

[39] Ictère Hemolytique Chronique, Avec Splenomegalie, Gaz. Heb. Sci. Méd. de Bordeaux, 1909, xxx, 469.

[40] Chronischer Ikterus mit Milztumor ohne Bilirubinurie, Casopis Lekaru, ceskych., 1906, p. 1029. (Ref. Schmidt's Jahrb., 1907, cexciv, 160.)

[41] Familial Milz und Leber Vergrösserungen mit Anämie, und Gutartiger Verlaufung, Deut. med. Woch., 1909, xxxv, 1749.

[42] Chronische Acholurische Icterus mit und ohne Milztumor, Berl. klin. Woch., 1907, xliv, 1065.

In favor of the identity of the two types it must be admitted that a series of cases could be selected in which many grades between the two types could be represented. It is obvious also that the familial type must at one time or another have originally been acquired. In such an event the difference in severity between the acquired and familial still holds. Thus both in Roth's[43] and Bychorski's[44] cases the disease in the parent who acquired it was severe, while in the children who inherited it, it was of the usual mild type. Such facts, however, would not indicate a fundamental difference in the nature of the two diseases.

In the small number of cases already accumulated, various atypicalities have been reported. Thus, Lommel's[45] and Claus and Kalberlah's[46] cases of the familial type, and Mosse's[47] and Tixier's[48] cases of the acquired type failed to show any change in resistance of the red cells (either washed or of the whole blood), though other evidences of increased blood destruction were present. In a few cases also a similar acholuric jaundice with splenomegaly has existed together with polycythemia instead of anemia. A slightly different form has also been described by Chauffard and Vincent,[49] Van den Bergh[50] and Roth,[51] in which homolysins are present in the blood, which, so to speak, occupies a midway position between hemolytic jaundice and paroxysmal hemoglobinuria "a frigore." Gibert[52] and his pupils have published numerous reports since 1900 on similar conditions under the name of "cholemie familiale." They have at least served to call attention to the fact that variations may be found in the amount of enlargement of the spleen and liver. It is questionable, however, if it is necessary, as they have frequently done, to consider each atypical form as a separate condition to be dignified with a separate name. As many of their cases were described before the various hematological methods above described had come into vogue, and are frequently reported in resumé, it is difficult to tell for sure whether or not they should be considered as belonging to the types under discussion. Their theory of hepatic origin, due to an infectious angiocholitis, was later abandoned by them in favor of Chauffard's idea that the primary change was in the blood.

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[43] Loc. cit.

[44] Zur Kasuistik der Heredofamiliaren Splenomegalien, Wien. klin. Woch., 1911, xxiv, 1519.

[45] Ueber die Sogenannte Bantische Krankheit und den Hemolytischen Ikterus, Deut. Arch. f. klin. Med., 1912, cix, 174.

[46] Ueber Chronischen Icterus, Berl. klin. Woch., 1906, xliii, 1471.

[47] Zur Lehre der Krankheiten mit Gesteigertem Hämolyse, Berl. klin. Woch., 1913, l, 684.

[48] Ictere d'origine Hemolytique, Resistance des Hematics Desplasmatisées Sensiblement Normale, Comp. Rendu de la Soc. de Biol., 1908, lxiv, 43.

[49] Hemoglobinurie Hemolysinique avec Ictère Polycholique Aigu, Semaine Méd., 1909, xxix, 601.

[50] Ictère Hemolytique avec Crises Hemoglobinuriques, Fragilité Globulaire, Rev. de Méd., 1911, xxxi, 63.

[51] Zur Frage des "Ictère Hemolysinique" (Chauffard), Deut. Arch. klin. Méd., 1913, cx, 77.

[52] Loc. cit.

All the symptoms of increased blood destruction may be present and yet icterus be absent. Thus, Chauffard describes a family in which the mother is a typical hemolytic icteric, while the eighteen-year-old son presents all the signs except the jaundice.

When the anemia is grave the blood may present a picture indistinguishable from pernicious anemia (v. Stejskal).[53] Chauffard considers that there is an icteric form of pernicious anemia which, when accompanied by diminished resistance and reticulated red cells, represents the least compensated form of hemolytic icterus. Widal and Weissenbach[54] have also reported a case of this type. In the usual Biermer type of pernicious anemia, icterus is absent and the resistance of the red cells increased.

Banti[55] has recently proposed the name hemolytic splenomegaly for a type of case which on analysis is indistinguishable from the acquired form of hemolytic jaundice. The two cases described by him (one an aplastic subvariety) both exhibit a chronic anemia, with long-standing splenomegaly, subicterus, diminished resistance of the red cells, increased number of reticulated cells, and urobilinuria. The beneficial effects of splenectomy, abolishing the anemia and changing the resistance to normal—in one case even changing an aplastic into a reacting bone marrow—lead him to ascribe a primary role in this disease to the spleen. It must be remembered, of course, that removal of the normal spleen indirectly causes an increase in resistance of the red cells. Banti claims never to have seen Widal's crises of deglobulization in these patients, and emphasizes the presence of a relative lymphocytosis; but this would hardly indicate a different disease. As to the choice of name, Banti's is open to the same objection as the other, namely, that splenomegaly may be absent in some cases (Le Gendre,[56] Pick,[57] Gilbert,[58] Benjamin and Sluka's third case, and Marchiafava and Nazzari[59]) just as jaundice is in others. A name indicating increased blood destruction, such as hemolytic hypersplenism, without including individual features, would be less open to objection; but in the meantime the name sanctioned by usage is preferable.

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[53] Uber Hemolytischen Icterus und uber den Auftreten Hemolytischen Vorgänge bei diesem und bei Perniciöse Anämie, Wien. klin. Woch., 1909, xxii, 661.

[54] Anémie Pernicieuse Cryptogenetique avec Hemolysinhémie et Fragilité Globulaire Alternante, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1913, xxix, 250.

[55] La Splenomegalia Emolitica, Sperimentale, 1912, lxvi, 91; La Splenomegalia Emolitica Anemopoietica, Sperimentale, 1913, lxvii, 323.

[56] Deux observations d'Ictère Hemolytique l'un Congenitale l'un Acquis, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1909, xxvii, 112.

[57] Ueber hereditärischem Ikterus, Wien. klin. Woch., 1903, xvi, 193.

[58] Loc cit.

[59] Sugli Itteri Emolitici, Bull. d. Reale Accad. di Roma, 1909, xxxv, 152.

PATHOGENESIS. As I have already indicated in the discussion of the differentiation of the two types, an hepatic or luetic etiology has been largely discarded for the idiopathic primary types. There remain the two views, that the primary lesion is in the blood, a dystrophy of the red cells; or either primarily or indirectly in the spleen, an exaggerated hemolytic activity. Widal and his school, the extreme supporters of the former view, consider that the congenitally weak red-blood cells are destroyed in the circulation and their remains taken up by the spleen (causing a spodogenous tumor) and by the liver, kidney, and bone marrow (hence the excessive pigment found in these organs at autopsy). This view was supported by Vaquez,[60] von Stejskal, Benjamin and Sluka, Aschenheim[61] and Weber and Dorner.[62] The chief objection to it is that it completely ignores the great improvement following splenectomy. A primary increased hemolytic activity of the spleen as the source of the malady was first proposed by Minkowski and supported by von Krannhals and Chauffard. Its latest adherent, Banti, as I have previously stated, considers that the pathological spleen not only is spodogenous, but actively destroys increased numbers of cells and prepares others for destruction. Though based on incorrect and inadequate experimental evidence, this attractive combination of the splenogenous and hemocatatonistic theories at present seems most plausible. Although it is not possible to demonstrate hemolysis by the normal spleen, we cannot exclude the possibility that that organ may in such diseased conditions, as Banti claims, take on increased hemolytic activity. Extracts from the spleens of Antonelli's[63] and Kahn's[64] cases, however, failed to show any hemolytic activity.

Whatever the source of the increased blood destruction may be, there results an increased amount of hemoglobin to be got rid of. The majority of authorities believe that it is changed by the liver into bile in excessive amounts, viscid and highly pigmented, which clog the bile capillaries, are resorbed into the blood, and thus cause a "pleichromic icterus." Recent investigations by Whipple,[65] however, show that bilirubin can be formed by the action of endothelium of bloodvessels entirely isolated from the hepatic circulation.

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[60] Ictère chronique acholurique avec splenomegalie, Bull. et. Mém. Soc. Méd. Hôp. Par., 1907, xxiv, 1184; Sur l'Anatomie Pathologique de L'Ictère Hemolytique, Arch. des Mal. de Cœur., 1908, i, 609.

[61] Ueber Familiären Hämolytischen Ikterus, Münch. med. Woch., 1910, lvii, 1282.

[62] Four Cases of Congenital Acholuric So-called Hemolytic Jaundice in One Family, Lancet, 1910, i, 227. Acquired Chronic Acholuric Jaundice, AMER. JOUR. MED. SCI., 1909, cxxxviii, 24.

[63] Intorno all'Effetti della Splenectomia su Ittero Emolitica Acquisita con Anemia a Tipo Perniciosa, Policlinico (Par. Med.), 1913, xx, 3.

[64] Loc cit.

[65] Icterus, Jour. Exp. Med., 1913, xvii, 612.

If this be true a hematogenous icterus in the narrower sense can be accepted. That the jaundice is not due to gross obstruction is proved by the facts that such obstruction has never been found, that the stools are of normal color, and that the urine does not contain bilirubin.

It is interesting to note that in Banti's aplastic or anemopoietic case, splenectomy started the regenerating powers of the bone marrow as shown by the appearance of normoblasts in the circulating blood. This would indicate that with the spleen there was removed a toxin that had inhibited blood formation and would argue that the weakened red cells of hemolytic jaundice are due, not to hemocatatonistic action of the spleen, but to an indirect injury to the bone marrow.

PATHOLOGY. Of the comparatively few cases that have come to autopsy or splenectomy a study of the morbid anatomy has not been very productive. I have collected eight autopsies and seven splenectomies, with the results shown in table on opposite page.

THERAPEUTICS. Views as to the treatment of these conditions have changed fundamentally in the past few years. Following Vaquez and Giroux's[66] case, in which death ensued two days after splenectomy, came Chauffard's dictum that hemolytic jaundice constituted a "Noli me tangere" for the surgeon. Various surgical attempts on the bile passages (Chauffard and Troisier;[67] Marchiafava and Nazzari; Widal, Abrami and Brulé); *x*-rays (Benjamin and Sluka); bone marrow feeding (Chauffard, Widal); cholagogues (Chauffard, Cavazza)[68] all proved unavailing. Only with a long-continued course of iron diet did Widal find some improvement. On account of the antihemolytic properties of arsenic (Gunn and Feltham)[69], cholesterin (Chauffard and Grigaut,[70] Parisot and Heully[71]), and calcium chloride (Iscovesco[72]), these drugs have been tried, in some cases with improvement, apparently due to increasing the resistance of the red cells. No curative measure had been produced, however, when splenectomy was again tried in 1911, with very different results. In that year Micheli removed the spleen from a case of the acquired type, with the most striking improvement; the blood count which had been between 980,000 and 2,600,000 quickly rose to almost normal, the acholuric jaundice and urobiliburia disappeared, the fragility of the red cells was lessened, and the patient within a few months was apparently

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[66] Ictère chronique acholurique avec Splenomegalie, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1907, xxiv, 1184.

[67] Des Rapports de Certaines Anemies Splenomegaliques avec L'Ictère Hemolytique Congenitale, Bull. et Mém. Soc. Méd. des Hôp. de Paris, 1909, xxvii, 293.

[68] Gli Itteri Emolitici-Milano, 1911.

[69] The Antihemolytic Power of Arsenic, British Med. Jour., 1911, i, 134.

[70] Le Taux de la cholesterinemie au cours des cardiopathies, Comp. Rend. Soc. Biol., 1911, lxx, 108.

[71] Le Traitement des Ictères Hemolutiques, Semaine Méd., 1913, xxxiii, 85.

[72] Les Lipoides du Sang. La Cholesterine, Comp. Rend. Soc. Biol., 1908, lxiv, 101. See also ibid., 1907, lxiii, 744.

TABLE II. PATHOLOGY OF HEMOLYTIC JAUNDICE.

Author.	Type.	Based on	Weight of spleen.	Capsule and trabeculæ.	Pulp.	Sinus.	Malpighian follicles.	Pigment in spleen.	Phagocytes in spleen.	Pigment in liver.	Bone marrow.	Miscellaneous.
Minkowski	Familial.	Autopsy.	Gms. 675	Normal.	Congestion.	Congestion.	. . .	Increase.	Increase.	Increase.	Red.	Much pigment in kidneys.
Vaquez and Giroux	Familial.	Autopsy.	850	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.	Normal.	Red.	
Gandy and Brulé[73]	Familial.	Autopsy.	750	Normal.	Marked congestion.	Congestion.	Normal.	Slight increase.	Increase.	Normal.	Red.	
Marchiafava	Familial.	Autopsy.	270	Thick.	. . .	. .	Necrotic.	Increase.	. . .	Increase.	. . .	Spleen slightly fibrotic.
Oettinger[74]	Acquired.	Autopsy.	575	Normal.	Marked congestion.	Congestion.	Small.	Increase.	Increase.	Increase.	Red.	Much pigment in kidneys.
Micheli	Acquired.	Autopsy.	850	Thick.	Congestion.	Congestion.	No germ centres.	Increase.	Slight increase.	Normal.	Red.	Endothelial cells of spleen increased. Liver fibrotic.
Kahm 1	Familial.	Operation.	970	Normal.	Congestion.	Congestion.	Normal.	Increase.	. . .	. . .	. . .	Few pulp cells in spleen.
Kahm 2	Familial.	Operation.	1170	Thick.	Congestion.	Congestion.	Few.	Slight increase.				
Umber	Acquired.	Operation.	1300	Normal.	Congestion.	Congestion.	Pigmented and congested.	Increase.	Increase.			
Antonelli	Acquired.	Operation.	1000	Normal.	Congestion.	Congestion.	Normal.	Increase.	Increase.			
Fiori	Acquired.	Operation.	1000	Normal.	Marked congestion.	Congestion.	Normal.	Increase.				
Banti 1	Acquired.	Operation.	1580	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.			
Banti 2	Acquired.	Operation.	970	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.	. . .	. . .	Endothelial cells of spleen necrotic.
Gaisböck	Acquired.	Autopsy.	?	Normal.	Not congested.	Not congested.	?	Increase.	Increase.	Increase.	Red.	Myeloblasts in liver and spleen.

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[73] Gandy, C., and Brulé, M. Ictère Hemolytique Congenitale Autopsie, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1909, xxviii, 369.

[74] Oettinger, W. Sur un Cas d'Ictère d'Origine Hemolytique non Congenitale, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1908, xxvi, 391.

cured. Similar beneficial results were obtained by Banti in his two cases of hemolytic splenomegaly, which I have taken to be identical with the acquired form of hemolytic jaundice. In the past two years splenectomy has been performed successfully in both acquired and familial types in cases reported by Antonelli, De Castello, Kahn, Lankhout,[75] Fiori[76] and Eppinger.[77] In no cases were there any bad results, and all showed a great improvement in symptoms, with specific evidence of lessened blood destruction. It is, of course, too early to know whether the improvement is but temporary or whether permanent cure has been effected.[78]

With such gratifying results and the analogous hyperthyroidism in mind, it is not surprising that the procedure should be applied to related conditions such as hypertrophic cirrhosis and pernicious anemia. Eppinger[79] considers that the amount of hemolysis in a given case can be determined by the iodin count of the blood fat (normal 80 to 90) and the amount of urobilin in the feces (normal 0.12 to 0.15 gm. per day). He found both these increased not only in hemolytic jaundice, but also in pernicious anemia, hypertrophic cirrhosis, and catarrhal jaundice. As he and King had found experimentally that removal of the spleen caused a great drop in the iodin content, (*i. e.*, lessened hemolysis), he proposed splenectomy in this type of case also. His latest theory of the pathogenesis of pernicious anemia is more fanciful. Having found thickened walls in the arterioles of the spleen, he assumes that the blood seeks the path of less resistance through Weidenreich's open capillaries into the pulp, where they are destroyed. Splenectomy therefore becomes equivalent to tying off a ruptured bloodvessel. This theory has not yet received widespread acceptance.

Klemperer's[80] summary of ten cases shows that the operative risk in pernicious anemia is considerable, and if successfully passed, an improvement which is not fundamental is the most to be hoped for. It is noteworthy that he bases the procedure on the incorrect hypothesis that splenectomy normally causes an increase in the number of red cells. Huber,[81] De Castello[82] and Mosse have also found improvement after splenectomy in an icteric type of pernicious anemia. It is interesting that in Huber's case the blood cells from the splenic vein showed no decrease in resistance. As all three patients had icterus, urobilinuria, fragility of corpuscles, and splenomegaly it is probable that these cases really belong to the class of hemolytic jaundice.

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[75] Hemolytische Splenomegalia, Nederl. Tijd. d. Geneesk., 1913, lvii, 1153.

[76] Un caso di Splenomegalica Emolitica Trattata colla Splenectomia, Sperimentale, 1913, lxvii, 189.

[77] Zur. Pathologie der Milzfunction, Berl. klin. Woch., 1913, l, 1509 and 2409.

[78] Since the above was written, the patient to whom I have previously referred has also successfully undergone splenectomy, with great improvement of clinical symptoms and return of blood picture almost to normal. His case with metabolic studies before and after splenectomy will shortly be reported by Pearce, Pepper, and Goldschmidt. The results of splenectomy in hemolytic jaundice have very recently been collected by Elliott and Kanavel (Surg., Gyn. and Obstet., 1915, xxi, 21). Of 48 cases splenectomized, 2 have died, and in the 46 "cures," practically all symptoms of the disease have disappeared.

[79] Loc. cit.

[80] In welcher Krankheit Kommt die operative Entfernung der Milz in Frage? Ther. d. Gegenwart, 1914, lv, 1.

[81] Ueber die Blut Veränderungen bir Icterus Hemolyticus, Berl. klin. Woch., 1913, l, 681 and 2179.

[82] Ueber den Einfluss der Milzextirpation auf der Perniciöse Anamie, Deut. med. Woch., 1914, xl, 639.

One might say in summarizing that splenectomy should be considered in all those diseases where there is evidence of increased blood destruction and that in early Banti's disease and hemolytic jaundice at least the results of splenectomy have been excellent. All such procedures, however, should be entered upon most conservatively as long as so much of the physiology of the spleen remains unknown. Though its removal is known to be compatible with life, it may yet prove to have such important detoxicating relations to infection or to digestion, that splenectomy should only be practised after most careful study and to relieve the most serious conditions.[83]

CULTURAL AND VACCINE RESULTS IN A CASE OF HODGKIN'S DISEASE.

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In the number of the *Archives of Internal Medicine*, for August, 1913, Bunting and Yates report six cases of Hodgkin's disease, from the lymphatic glands of which they have isolated a diphtheroid organism considered by them as identical with the one described by Fraenkel and Much.[1] In 1900 the last-named authors were able to extract Gram-positive, non-acid-fast, diphtheroid bacilli from the sediment of the lymph glands which had been previously treated with antiformin, to which preparation the organism was resistant.

Negri and Mieremet[2] were the first to report successful cultivation of this organism, isolation of which was brought about on Bordet's medium (blood-glycerin-potato-agar).

Billings and Rosenow[3] have isolated the same organism from eighteen cases of Hodgkin's disease, the glands of which were diagnosed microscopically. The majority of the cases show the glands to be of the endothelioid type described by Reed and Longcope. They report favorable vaccine results in some of the cases, practically all of which were simultaneously treated with the Roentgen-ray. This agent, as is well known, often causes decrease in the size of the cervical glands, but as a sequel to this treatment the thoracic and retroperitoneal nodes seem to develop faster.

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[83] Since the above was written, numerous reports of splenectomy for pernicious anemia have appeared. Though the patient's general condition was improved temporarily in many cases, in no case has definite cure resulted, or the blood picture of pernicious anemia been fundamentally changed.

[1] Ztschr. f. Hyg., 1910, xvii, 189.

[2] Centralblatt f. Bak., 1913, lxviii, 292.

[3] Jour. Amer. Med. Assoc., December, 1913.

Since every case of this disease that reacts favorably or unfavorably to an autogenous vaccine is of value, I feel justified in reporting this single case, even though my vaccine results are distinctly unfavorable:

The patient under consideration was a male, aged fifty-seven years. He had worked as a carpenter all his life. He was first seen May 8, 1915, and gave the following history: About one year ago he noticed a stiffness in the back of his neck which could never be made to disappear completely, and which was aggravated by slight chilling. Three months later he noticed a gland under the right tonsil somewhat enlarged, and accidentally discovered two small kernels in the occipital region. In February, 1914, other glands appeared on the right side of the neck, with a beginning involvement in a similar location on the opposite side. They had all been of rapid growth, were painless, and were freely movable under the skin. The tonsils were not greatly enlarged, and no history of repeated tonsillitis or sore throat was obtainable. The Wassermann reaction, urinalysis, and von Pirquet test were negative. The blood findings were as follows: reds, 4,900,000; whites, 10,200; hemoglobin, 89 per cent. A differential count of 500 cells shows: polymorphonuclears and transitionals, 62 per cent.; lymphocytes, 20 per cent.; large mononuclears, 14 per cent.; eosinophiles, 4 per cent.; no myelocytes or basophiles. No pathological changes in the red cells.

May 8, 1914, a lymphatic gland, with capsule intact, was removed from the right submaxillary region under local anesthesia. This will be known as R I. It measured 2 x 3½ cm., and had been growing for about three months, attaining most of its size in the last month.

On the left side the most recently involved gland was removed. It was located at the level of the cricoid cartilage under the sternomastoid. An incision was made in this muscle, and under moderate pressure from the forceps this gland, which was decapsulated, accommodatingly popped up through the incision. Its size was 1 x 2 cm. It was transferred directly to a tube of whole blood glucose agar. It will be known as L I. There was also removed from the same location a circular node recently involved, and about 6 mm. in diameter. It will be known as L II.

A pathological examination of the glands showed the following changes: For the most part the histological architecture of the gland was destroyed. There was marked lymphoid hyperplasia in addition to a striking hyperplasia of the endothelial cells lining the lymph sinuses. A few multinucleated bizarre-shaped endothelioid giant cells were present, but no eosinophiles were observed. A diffuse sclerosis was just beginning. In some parts of the early nodes the arrangement of the gland had not been disturbed, and the proliferation of the endothelial cells lining the sinuses gave the appearance of densely packed cords of cells. In other areas only the lymphoid hyperplasia was noticeable.

Gland R I was washed in sterile normal salt solution and transferred to a sterile Petri dish. It was longitudinally incised and divided into three parts. The following disposition was made of the sections: A suitable portion was placed in formalin for pathological examination, the result of which has just been described. A second portion was placed in a sterile mortar and ground in sterile air. An emulsion was made in sterile normal salt solution and was planted on fifteen tubes of different kinds of media. The results of these cultural findings are not detailed in this article because they were the same in substance as were derived from the third portion of the gland, the results of which are detailed in the protocol. This portion was cut into small pieces and planted on several tubes of the following kinds of media: (1) 2 per cent. glucose agar, plus 10 per cent. beef serum; (2) 2 per cent. glucose bouillon plus 10 per cent. beef serum; (3) 2 per cent. glucose agar plus 5 per cent. whole human blood; (4) 2 per cent. glucose bouillon plus 10 per cent. ascitic fluid; (5) 2 per cent. glucose agar plus 5 per cent. whole human blood, about three weeks old. These media were incubated forty-eight hours before their use in these experiments. For the sake of convenience and brevity these different varieties will be referred to as Media 1, Media 2, etc., in the protocols.

An examination of the protocols of the cultural results discloses several things of interest: The marked pleomorphism of the organism has been mentioned by Bunting and Yates, and it is indeed one of its striking as well as its confusing features. Some of the diphtheroids are very large, these usually being club forms or ones heavily barred. Others are short and thick, corresponding to the solid type of the diphtheria bacillus. Under certain conditions the coccoid forms of varying size and staining power are developed. Branching forms were not uncommon. Some have a long, terminal filament, usually wavy in character. This may branch, or it may give rise to a more or less complex network which when stained by Gram's method is easily decolorized. Many of the coccoids have shorter spicules or projections of this character, while the wavy, pale filaments may also be seen free in the smears, and which show the above-mentioned characteristics. All these forms usually disappear in the transplants. The filaments are interesting in relation to the supposed spirochetes seen by Proescher and White[4] in Hodgkin's glands, and thought by them to be the etiological factor in the disease. Their observations have not been generally confirmed. These filaments may also throw light on the origin of the spirochetes of Vincent's angina. They have never been cultivated, and are supposed by Tunnicliffe[5] to be outgrowths of the fusiform bacillus of this condition. They can usually be seen as thin, wavy filaments attached to one end of the bacillus in a well-stained preparation.

There was considerable variation in the gross features of the cultures. On blood-agar the growth began, as a rule, in the water of condensation. It grew slowly on the slant, appearing for the most part as a moist dewdrop formation, thus resembling the Streptococcus pyogenes. Later it turned a light gray color and grew more luxuriantly. It had a decided preference for a moist surface. It would lie dormant for some time on the surface of a dry medium, but would grow readily when a little distilled water or sterile salt solution was added to the medium. Not infrequently the individual transplanted colonies would become opaque with unequal intensity, giving the colony a stippled appearance. On beef serum and plain glucose agar the growth was slow and sparse, but became more luxuriant with frequent transplants. The cultures gradually became chromogenic, producing first a yellow and later an orange or pink pigment. One culture transplanted May 26, 1914, in gelatin was viable December 1, having developed an orange pigment. The bacillus was decidedly aërobic, spreading arborescently over the surface of the gelatin in sunflower fashion, while the beaded growth along the stab had not perceptibly progressed. The viability was best preserved on gelatin.

Bouillon was diffusely clouded during the first few hours of growth, but soon cleared up, giving rise to a moderate quantity of fine granular sediment, collecting along the sides and on the bottom of the tube. When beef serum was added to the glucose bouillon the tendency for the organisms to clump was quite noticeable.

Neither glucose nor lactose was fermented, nor was a trace of acid produced even when using such a delicate indicator as Andrade's reagent[6] (decolorized acid-fuchsin).

The organism was resistant to antiformin and was non-acid fast. It stained faintly in Loeffler's, but easily with gentian violet and carbolfuchsin. The best differentiation was brought about by the method of Gram, to which it reacted strongly under favorable conditions. But any change of environment had a remarkable effect on its power to retain this stain.

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[4] Münch. med. Wchnschr., 1907, liv, 1868; Jour. Amer. Med. Assoc., 1907, xlix, 1115.

[5] Jour. of Infect. Dis., 1906, iii.

[6] Annual Report United States Marine Hospital Service, 1895, p. 385.

In general it can be said that the growth on old blood agar and on dry media caused a large number of the organisms to be decolorized. In the condensation water of cultures a week old such changes could easily be seen. In some cultures all grades of reaction to this stain might be seen; in others, the entire culture was finally decolorized. Prolonged growth on the simple media was also favorable for the retention of this stain. However, when the coccoid bodies were developed by any of these processes they were much more constant in their positive reaction to the Gram stain than were the bacilli. The reasons for these deductions can be seen by consulting the protocol.

May 15, 1914. L I.
May 14, 1914. Transplant 2.
May 21, 1914. Transplant 11.
May 15, 1914. L I, both slant and water of condensation.
May 15, 1914. Transplant 19, L I.
May 16, 1914. Transplant 26, L I.
May 13, 1914. Transplant 8, L II.
May 22, 1914. Transplant 31, L I, condensation water.

Another point of interest toward which attention was directed, lay in determining whether the cocci or coccoid forms were derived from the bacilli or represented a separate bacterium. By first shaking up the organisms with sand, and then plating them out by the dilution streak method, isolated colonies containing no coccoids were found. When transplanted under unfavorable conditions, an abundance of these forms appeared. (See plate cultures I, II, and III, under subcultures of gland L I.) In addition it will be seen that gland L I and L II contained none of these when the growth first started. By following the examinations of the condensation water of L I from day to day a progressive shortening of the organism was seen, until finally many of these anomalous forms appeared. One tube of gland L II which had contained no coccoids, ran along for several days without change, either macroscopically or microscopically. Then from May 15 to May 16 the growth suddenly changed from a transparent dewdrop character, to a more luxuriant opaque formation. Microscopically, practically nothing but coccoids were found. (See L II, May 16.) Other reference to protocols bearing on this point are transplants No. 3, May 12 and May 14; transplant No. 16 of May 14; transplants Nos. 14 and 15, of May 18.

It seems probable that the coccoids represent involution forms of the bacillus, as they flourish under an unfavorable environment. If, for example, the organism grows on a medium which delays its appearance, or on a stale or dry medium, coccoids appear quickly. The age of the cultures also has a decided bearing, especially if it be on one which degenerates rather rapidly, *e. g.*, blood agar. (Under L I protocol, see description under date of May 13 and May 15 (Plate I). Transplant II of May 21, 1914; transplant 19 of May 15, 1914; transplant 25; transplant 35 tube (3) of L I, May 18, 1914; under L II see transplant 8, and under R I see tube number 5, May 15, 1914; transplant 9 of May 12, 1914.

Attempts to have the coccoids develop in chains failed. (Transplants 40 and 41.) No true spore formation or motility was observed. Gelatin was not liquefied, but was the best medium among those I used to preserve the viability. Large involution spherical forms were present in old cultures of this medium, which were usually chromogenic.

No attempt was made to enter into all the details of morphology, and the cultural and biochemical characteristics which go to determine unequivocally the location of the organism in its proper place. Only those were entered into which would suffice reasonably for its identification as described by those who first isolated it. However, the apparently rare filamentous forms and its chromogenic capacity were novel to me.

PATHOGENICITY. May 18, 1914, a guinea-pig and a rabbit were each injected with a salt suspension of 1 c.c. of the bacillus from the right gland into each thigh subcutaneously. A rabbit and a guinea-pig were also treated with 1 c.c. of the suspension from the left gland. This time the injection was made subcutaneously into the right thigh, and also intraperitoneally, 1 c.c. being given in each place.

None of the animals showed symptoms, but the rabbit which received the injections in two locations soon lost the extreme vivacity which had characterized her heretofore. Progressive diminution in weight and strength occurred until October 20, 1914, at 5 P.M., when the animal died in an extremely emaciated condition. (Original weight, 1940 grams; antemortem weight, 860 grams.) No rise in temperature was observed at any time.

Autopsy, October 20, at 6 P.M. Smears were made from all organs, but were negative. Parts of the lung, liver, heart, kidneys, spleen, and ovaries were placed in formalin and subjected later to a pathological examination, which was negative. Lymphatic involvement was also negative. Parts of the organs were planted on blood agar. Results were negative except with an ovary, which after five days yielded on the slant two small gray colonies, which proved to be diphtheroids of the same character morphologically as the ones injected. The condensation water surrounding the tissue was rich in the same organism.

On transplants to blood agar the organism grew in light gray colonies after forty-eight hours. It was a strongly Gram-positive, non-acid-fast diphtheroid. It produced no acid on glucose and did not liquefy gelatin. It was decidedly pleomorphic, following the same general lines as its supposed antecedent, except that no coccoid forms have been observed up to this time.

Cultures of it have been injected daily into rabbits for a month, but so far the animals have shown no significant signs. Animal experiments with both organisms are being continued.

VACCINE TREATMENT AND SUBSEQUENT HISTORY. Vaccines were prepared from the bacilli of both glands and from the coccoid forms of the left gland cultures. The organism was grown forty-eight hours on glucose-agar, washed down in normal salt solution, filtered through glass-wool-cotton filter to remove clumps, heated to 56° for one hour, after which 0.1 formalin was added. Controlled for four days on blood agar.

May 25, at 11 A.M., five millions of the killed bacilli of gland L I were given subcutaneously into the left arm. No temperature; no local, focal, or constitutional reaction.

May 28, ten million bacilli given in the same manner. Glands of right side given a mild Roentgen-ray treatment. No reaction of any sort.

May 30. Some improvement. He turned his head more easily; all palpable glands receded slightly and the patient felt generally improved.

May 31. At 8 A.M., fifteen millions of the dead organisms from L I were given. No reaction of any kind. No improvement in his condition. In fact, the glands in the cervical region were gradually enlarging and the axillary glands on the right side, and the inguinal glands on both sides were involved. A Roentgen-ray treatment given, but no improvement resulted.

June 8. A vaccine of 25,000,000 given subcutaneously. He returned home until July 13. During this time he received three doses of vaccine, the sizes of which were 50,000,000, 75,000,000, and 85,000,000. He was not under my control at this time, but was treated by his home doctor. He reported no improvement from any of the vaccines. The dose of 85,000,000 produced a rise in temperature of 3°, which receded in forty-eight hours. The glands continued to enlarge.

July 13. I administered a dose of 150,000,000. He had only a slight temperature rise, but his condition did not change.

He did not return for further treatment, but went to Chicago some time later, where he was treated by Dr. E. C. Rosenow. From him I learned that an axillary gland had been removed and a vaccine prepared. I next heard from his home town that he died about September 1.

In this case I am unable to see any good results whatever that can possibly be traced to his autogenous vaccine, although the dosage did not go above 150,000,000. Excepting a few transitory improvements, which might be traced to the Roentgen-ray, his downward course was a rapid and uninterrupted one from May 8 until July 13, and his demise six weeks later would seem to conform to the previous rapidity with which the disease progressed. I might add that the removal of the glands by surgical operation caused a rapid enlargement of the neighboring glands. I can only hope that my case was atypical and that the general run of the cases will yield to treatment.

PROTOCOL OF CULTURAL RESULTS.

Media No. 1—Two per cent. glucose agar plus 10 per cent. beef serum. May 9, 1914: No growth. May 10, 1914. No growth. May 11, 1914: No growth.

Media No. 2—Two per cent. glucose bouillon plus 10 per cent. beef serum. May 9, 1914: No growth. May 10, 1914: The bouillon is diffusely clouded. Microscopically bacilli of varying size and shape are found. Many solid and barred types, while a few have bipolar granules. A few coccoid forms are present. Stain well with Gram but faintly with Loeffler's. May 11, 1914: A heavy white precipitate is deposited at the bottom of the tube, while the supernatant fluid is clear. No change microscopically.

Media No. 3—Two per cent. glucose agar plus 5 per cent. whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 4—Two per cent. glucose bouillon plus 10 per cent. ascitic fluid. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 5—Two per cent. glucose agar plus 5 per cent. whole human blood (three weeks old). May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Left Gland L I.

Media No. 1—Two per cent. glucose agar plus 10 per cent. beef serum. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 3—Two per cent. glucose agar plus 5 whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 5—Two per cent. glucose agar plus 5 per cent. whole human blood (three weeks old). May 9, 1914: Negative. May 10, 1914: The cloudy fluid surrounding the piece of gland shows the same findings as occur in the bouillon from the right gland, except no coccoid forms are present. Gram-positive. May 11, 1914: Increase of turbidity in the condensation water. This was permitted to run over the slant of agar. See transplants 2. 10, 11, 19, 22, 23, 25, 26, 31, 32, 33, 35, 40, 41, 42 under protocol of subcultures, L I.

Left Gland L II.

Media No. 3—Two per cent. glucose agar plus 5 per cent. whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Gland R I.

Media No. 1—May 12, 1914: No growth. May 13, 1914: Growth appeared for first time. Many coccoid forms. Variation in reaction to Gram stain. May 14, 1914: No change.

Media No. 2—May 12, 1914: Increase of growth. No change microscopically. See transplants 1, 3, 4, 6, 7, 9, 16, 17, and 29 under Protocol of subcultures R I. May 13, 1914: No change. May 14, 1914: No change.

Media No. 3—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: First growth appears. Dewdrop formation. Diphtheroid and coccoid forms. Gram positive.

Media No. 4—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: Negative.

Media No. 5—May 12, 1914: First growth shows fine barred and solid bacilli. Gram positive. May 13, 1914: Growth first occurred as Gram positive bacilli and coccoids. May 14, 1914: Many barred forms.

Gland L I.

Media No. 1—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: Negative.

Media No. 3—May 12, 1914: Tube 41 shows fine, slender, long bacilli and coccoid forms. All are Gram positive. May 13, 1914: The slant shows many coccoids. Marked pleomorphism. The condensation water shows bacilli, narrower and shorter, but maintaining the granulation. Sparcity of coccoids. May 14, 1914: No change.

Media No. 5—May 12, 1914: The slant shows a thin, grayish, slimy growth. Microscopically, diphtheroid bacteria of great diversity of size and shape. Clubs, dumb-bells, and grotesque forms. Practically all have one or more deep blue granules located at the dilated end of the bacillus. Metachromism. Loeffler's stain negative, organisms are strongly Gram positive. May 13, 1914: Tube 2, L I. All coccoid bodies. Occur singly as diplococci, or in groups. Great diversity in staining power. This is first growth on Tube 2, L I. May 14, 1914: No growth as yet on slant. Turned condensation water over slant.

Left Gland L II.

Media No. 3—May 12, 1914: Negative. May 13, 1914: All bacilli as in Tube 1, L I. Dewdrop colonies on slant. See transplants 8, 13, 14, 15, 28, 30, 34, and 38. May 14, 1914: No change.

Gland R I.

Media No. 1—May 15, 1914: No change. May 16, 1914: All are Gram-positive coccoids.

Media No. 2—May 15, 1914: No change. May 16, 1914: No change. May 21, 1914: Most of the bacilli are Gram-negative. Some Gram-positive coccoids found.

Media No. 3—May 15, 1914: Many barred forms. Positive to Gram. May 16, 1914: No change.

Media No. 4—May 15, 1914: Negative. May 16, 1914: No growth occurred.

Media No. 5—May 15, 1914: No change. May 16, 1914: No change.

Gland L I.

Media No. 1—May 15, 1914: Negative. May 16, 1914: No growth occurred.

Media No. 3—May 15, 1914: Condensation water shows many Gram-positive coccoids, and many Gram-negative diphtheroid bacilli. May 16, 1914: Condensation water of L I contained small Gram-positive, barred bacilli.

Media No. 5—May 15, 1914: Fine dewdrop growth, just starting to turn gray. Strongly Gram-positive cocci. May 16, 1914: No change.

Gland L II.

Media No. 3—May 15, 1914: Forms are shorter and more of the solid type, but still bacilli. May 16, 1914: All Gram-positive cocci. The slant is no longer of dewdrop appearance, but is light gray.

PROTOCOL OF SUBCULTURES OF GLAND REMOVED FROM THE RIGHT CERVICAL REGION (R I).

First generation of subcultures.

May 12, 1914—Transplants 1 and 3 planted May 11. From Media No. 2 to fresh whole blood agar (Media No. 3). Both tubes show some heavy gray colonies and some that look like dewdrops. The former are Gram-positive, slender, long bacilli with marked granulations. Only a few club forms. Barred type predominates if the media is a little old or dry. The dewdrop colonies show the same bacteria.

May 17, 1914—Transplants: 6 and 7 from Media No. 2 to Media No. 1. Shows a pure culture of very large bacilli with most intense barring. No coccoid forms present. Protoplasm is light blue, but the bars are intense blue. Transplant 29 is from the incubated gland in the Petri dish on which colonies appeared first May 12. Planted on beef serum bouillon. A precipitate formed in the bottom of the tube. Supernatant fluid clear. No clumping. Shows Gram-positive coccoid forms.

May 15, 1914—Tube 5. First appearance of growth May 12. Single colony growing from a piece of gland tissue. Colony gray and has not spread laterally as much as in depth. Microscopically, short, fat Gram-positive bacilli of the solid type, as well as thinner curved Gram-negative filaments, which may or may not be bacteria.

Second generation of subcultures.

May 13, 1914—Transplant 4 from dewdrop colonies of transplant 1 to Media No. 2. Shows slender solid type bacilli. Gram-positive.

May 16, 1914—Transplant 9 from dewdrop colonies of transplant 1 to Media No. 5. Many coccoid forms mixed with slender bacilli. Variation in reaction to Gram stain. Some bacilli are greatly decolorized.

May 14, 1914—Transplant 16 from transplant 3 to Media No. 5. Shows Gram-positive barred and coccoid forms. Transplant 17 from transplant 6 to Media No. 1. Shows same forms as transplant 6. Transplant 18 from transplant 1 to Media No. 3. Dewdrop colonies. Microscopically, strongly Gram-positive, barred bacillus.

Part of right gland in Petri dish incubated at 37°, May 8. Small gray colonies appeared May 12. Mostly they are Gram-negative cocci, although a few are Gram-positive. Some colonies are very fine, slender bacilli, with coccoid forms which are Gram-negative.

Subsequent examination of previous subcultures.

May 13, 1914—Transplant 3. Still shows slender, long bacilli. Gray growth gradually becoming opaque.

May 14, 1914—Transplant 3 shows true coccoid forms, but little else. The individuals are quite large. There are many short, plump bacilli and some barred types. Compare description of same culture of May 12.

May 14, 1914—Transplant 6. No change. All Gram-positive.

May 16, 1914—Transplant 6. Very few are Gram-positive. Mostly Gram-negative, barred forms.

May 13, 1914—Transplant 1. Growth changed from dewdrop to gray, and colonies are opaquely stippled.

May 21, 1914—Tube 5, R 1, transplanted to beef serum. Very slow development. Fusiform and barred types. Only moderately positive to Gram.

May 21, 1914—Transplant 17. Large, barred bacilli. Some positive and some negative to Gram.

First generation on different media.

May 12, 1914—Transplant 2 from condensation water of L I on Media No. 3 to Media No. 3. An apparently pure culture of a bacillus, uniform in size and shape, with many Gram-positive, barred forms. Transplant 10 from the condensation water of L I to beef serum. (Media No. 1.) Many barred forms and some coccoids.

May 21, 1914—Transplant 11 from L I, May 13, to old blood agar. All are cocci of varying sizes. Some Gram-positive and some Gram-negative.

May 15, 1914—Transplant 19 planted May 14, 1914, from slant of L I to Media No. 5. Shows a fine dewdrop growth. Microscopically, shows coccoids, moderately Gram-positive.

May 16, 1914—Transplant 25 from agar slant L II on Media No. 3 to Media No. 1. Mainly small Gram-positive cocci, and a few bipolar bacilli.

May 17, 1914—Plate I. May 11, 1914, a dilution streak on Petri dish of Media No. 5 from condensation water of L I. No growth until plate was moistened with salt solution. Then the individual colonies appeared along the streak. An examination of individual colonies shows Gram-positive and Gram-negative diphtheroids in the same colony.

May 18, 1914—Plate III from condensation water of L I to Media No. 3, planted May 16. Same results as on Plate 1.

May 18, 1914—Transplant 35 from condensation water of L I, planted May 12, 1914 on Media No. 5. First growth May 17, 1914. Nothing but Gram-positive coccoids.

May 18, 1914—Transplant 31. Entire gland L I transplanted to Media No. 3 on May 16, 1914. Shows diphtheroids of remarkable diversity of form. They are strongly Gram-positive. Many drumstick forms are present, the stems of which are projected into long tails which stain Gram-negative. Sometimes these whips or tails branch simply, but at other times the arborization is almost dendritic. These Gram-negative filaments are also free in the smear. They may explain the apparent Gram-negative filaments or bacteria found in the other cultures. The oval coccoids often have tails at both ends. Some are Gram-positive and others Gram-negative. They resemble early Leishmann-Donovan bodies. Transplant 35. From condensation water of L I, planted May 12 on Media No. 5. Nothing but Gram-positive coccoids.

Second generation on different media.

May 16, 1914—Transplant 26, from transplant 23 to Media No. 3. Diphtheroids and coccoids which show all grades of reaction to Gram stain.

May 18, 1914—Transplants 32 and 33 from transplant 26 on Media No. 3. About same forms as described under transplant 31, excepting there are fewer coccoids and Gram-negative filaments.

May 18, 1914—Transplant Plate II. Transferred a colony of diphtheroids from Plate I to a plate of Media No. 1. Microscopically, they are all Gram-positive cocci of varying sizes. There are some bipolar bacilli, the bodies of which stain poorly with Gram.

May 18, 1914—Transplant No. 2, transplanted to Media No. 3 from original colonies of Plate I which were cocci. Microscopically nothing but Gram-positive cocci. Transplant No. 10 is from Plate III into human serum bouillon. In eighteen hours, growth shows cocci, but merely a suggestion of chain arrangement. Nothing definite. Transplant 41 from Plate III into beef serum bouillon. A very decided clumping of the cocci occurs. No suggestion of chain arrangement.

Subsequent examinations of subcultures L I.

May 13, 1914—Transplant 2. Slender, barred bacilli in the condensation water. No change.

May 14, 1914—Transplant 2. Great variation in the reaction to Gram-stain. Many bacteria are nearly decolorized.

May 22, 1914—Transplant 31. The slant shows many branching forms of diphtheroids. Gram-positive. The shapes are more regular in the condensation water, and do not hold the Gram-stain well.

May 18, 1914—L II, tube 3, planted May 8. First growth May 15. Almost all Gram-positive cocci. Very few diphtheroids.

Subsequent examinations of subcultures L II.

May 21, 1914—L II on Media No. 2. No change. All Gram-positive coccoids.

PROTOCOL OF SUBCULTURE OF THE SECOND GLAND REMOVED FROM THE LEFT CERVICAL REGION (L II).

First generation of different media.

May 13, 1914—Transplant 8 from L II Media No. 3 to Media No. 1. Short plump forms with small amount of barring and granulation. They are not Gram-negative, but are greatly decolorized.

May 17, 1914—Transplant 28 is from slant of gland L II into Media No. 2. Precipitate in the bottom of the tube, while the supernatant fluid is clear. Shaking yields a finely granular cloud. Marked clumping tendency. Transplant 30 is from L II slant into human serum bouillon. Same findings as transplant 28.

May 18, 1914—Transplant 34. L II planted on Media No. 1, May 15. Shows Gram-positive cocci. Transplant 38, from tube 2, gland L II which showed nothing but cocci on first examination. No change in this transplant.

May 18, 1914—Transplant 13, from transplant 28 to Media No. 1. All Gram-positive cocci. Transplant 14 and 15 are from transplant 28 to Media No. 5. Small Gram-positive coccoids. Some do not hold the stain well.

THE DIAGNOSIS BETWEEN PRIMARY AND SECONDARY ACUTE CARDIAC PICTURES.[1]

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It is with a full appreciation of the intimacy of the confidence imposed upon the consultant, and of the restrictions limiting the ownership of clinical data acquired under the relations of professional privilege and friendship, that I am venturing to sketch in barest outline four cases seen recently in conference with medical friends.

The first was of a man who complained of intense dyspnea on the slightest exertion in bed, of substernal oppression, of palpitation, and of sharp precordial pain. The pulse was feeble, slightly irregular, and in rate 120. The temperature was subnormal. The cardiac symptoms had impressed his physician to the extent of leading him to minimize the fact that the patient was breathing little, if at all, with his left side, which posteriorly showed unmistakable evidence of a bronchopneumonia, from which in due course he died.

The second patient was a young woman whose pulse rate, when I first saw her, was 130 and above on the slightest exertion. Even at rest it remained constantly about 110. She had been an excessive tea and coffee drinker, and had been in the habit of frequently using headache powders. She was of a highstrung, neurotic temperament, and the victim of long indoor hours, overworry, and work. When sent to me for examination she could hardly walk from the door to a chair. Palpitation and dyspnea were distressing, and were even worse when at rest in bed than when exercising. Moderate numbness and pain at times extended down the right arm. There was no cough, no sputum, no hemoptysis. She had been healthy until five weeks before. Her physician concluded that her case was one of neurasthenia. This patient's heart was found widely dilated to the right, left, and upward; both jugulars were pulsating in systole, and over the entire precordia could be heard a rough, short, systolic murmur. There was no edema. The lungs showed here and there a few subcrepitant rales due to congestion.

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[1] Read before the Section on Medicine, College of Physicians of Philadelphia, November 23, 1914.

The third patient was a young man who presented a series of clinical symptoms very similar to the preceding, except that he was large and robust of frame, whereas patient No. 2 was thin and frail. His dyspnea, palpitation, and general physical exhaustion had increased progressively during three months, until he himself was alarmed. He had previously been strong and well. His physician, a woman, sent him to me for examination primarily in order that sexual excesses might be determined or excluded as the basal factor in the case. The clinical picture was suggestive of myocardial incompetency. The physical examination did not dispel the likelihood of this supposition. But the boy's own frank admission of excessive sex intercourse, as well as the favorable outcome of the case, left no other conclusion possible than that the myocardium was and is normal and sound when permitted to perform its functions under the influence of sane nervous stimuli in a body nourished by internal secretions which were being squandered in riotous waste.

In the fourth and last case I was asked to examine the heart with a view to the possibility of a septic myocarditis. The patient was suffering at the time from a suppurating knee-joint and a large inguinal pus collection. His pulse was 110 to 120, his temperature had just touched 105° F., he was coughing, and spitting mucus and bright red blood. On examination it was evident that his heart was widely dilated, with active venous pulsation in the neck, and marked arrhythmia. The cardiac action was angry, but there was no murmur present. Very striking, however, at the first glance were the immobility of the entire left chest as compared with the laboring right side, and the shower of subcrepitant rales heard in the left axilla. There was undoubtedly present a septic congestion or (its later stage) a central bronchopneumonia, and the cardiac embarrassment was evidently to be attributed equally to it and to the causal toxemia.

The study of the foregoing and similar cases has led me for my own benefit, as well as for the advantage of others who may be placed in similar conditions, to attempt to formulate a working scheme for the discrimination between primary and secondary acute cardiac clinical syndromes.

I shall not consider at this time the relation between the heart and the kidney, or between heart insufficiencies and sclerosis of the vascular system. These fields are too extensive and present the conditions of chronic rather than acute disease. Moreover, their discussion would finally lead us to no definite agreement. I shall dwell briefly on such acute cardiac pictures as appear in neurotic states, in gastro-intestinal toxemias, in the pneumonias, in tuberculosis, in hyperthyroidism, in drug intoxications, and other systemic embarrassments that tend to obscure the real causal factor and to over- or underemphasize the heart.

At the close of a clinic a few days ago the question was asked, "How does it happen so often that the first signs of a pulnonary tuberculosis are heart or stomach symptoms?" This question graphically defines the aim and the limitations of this study. If we were to use slightly different words we might ask, "How often does the heart act as the spokesman for other organs; how can we make certain when it is speaking only for itself?"

There will, no doubt, be as many methods of procedure as there are individual examiners. It may even be that the most thorough and successful of all will formulate no definite scheme. If so he deserves no credit for his talent other than as the possessor of an inheritance by divine right. He is fortunate, but he has not earned his success. However, there are not many of him.

It is well to recognize the fact at the start that the discrimination is not always easy, and now and again is exceedingly trying and difficult. There are *two general conditions* in which we may find ourselves put to the test, and *two cardinal principles* upon which it appears to me rational to base our procedure. The first of the general conditions is exemplified in a patient experiencing cardiac symptoms in the presence of (though not necessarily due to) organic muscular or valvular disease of the heart. The second may be noted in one suffering from a cardiac syndrome in the entire absence of a recognized antecedent lesion, and perhaps in the presence of a heart, normal heretofore, and still normal under ordinary circumstances.

The first and by all odds the best *method* I could suggest would be a deliberate and complete ignoring of the heart in the preliminary physical examination and a studied effort to explain doubtful symptoms on other grounds than those of cardiac disease. Failing in this, and forced at length to consider the heart as the *origo et fons mali*, I would propose as the second step in the diagnosis a still further reluctance to attribute more of importance to the cardiac disease than is its due. Translated into other terms this means that we should continually remember the intimacy of the interrelation between the heart and every other of the thoracic and abdominal viscera, also the brain, and the influence of this interrelation upon the symptoms arising from these organs.

The functional integrity of every organ depends first, if not last, upon the origination of a tiny stimulus in the cardiac sinus node, upon its transmission through the several conducting pathways, and upon the heart's systolic output in suitable quantity of a nourishing blood supply. This being true, it will be easy for slight and secondary cardiac embarrassments to announce themselves in the language of either hungry or overfed heart-dependent organs. Standing on the threshold of a thoroughgoing reconstruction of the physiology of the heart and, consequently, of the physical diagnosis of cardiac disease, our task at once takes on a perplexing and tentative nature, and our doctrines must be correspondingly circumspect.

Confusion will most often come from the respiratory side. Fastened securely to the lungs above and behind by the pulmonary vessels and the pericardial reflections, and still more firmly to the diaphragm below by its pericardial union with the wall of the inferior vena cava, the heart experiences every movement of the lungs, one or both, and, in pulmonary affections, suffers not only from too much, but from an unsuitable form of exercise. The lungs expand from the apex downward, and in their excursion carry the heart downward from its normal position. As soon as the great veins are put under traction their supply of blood to the auricles is interfered with and the equilibrium and mechanism of the cardiac cycle at once has to pay toll. This interference with the veno-auricular flow is a far more vital menace than any mere mechanical obstruction in the pulmonary tissue. There can exist no room for doubt that an excessive number of the 30,000 and more air vesicles may be put out of commission by overdistention, or by crowding with exudate, or by rupture, or by collapse due to pressure from fluid or other cause without. These are, however, not the conditions that lead to serious acute mechanical disturbances. Very seldom do they, of themselves, cause fatality. The bacteremias and toxemias that cause these states are the vital factors threatening the heart, not the consolidations and the congestions and the edemas and the transudates and exudates of fluid, as a rule. Because of this fact both the myocardium and the gastric mucosa offer their early complaint in tuberculosis and pneumonia; and, for the same reason, not infrequently, the cardiac or the gastro-intestinal picture dominates the course of the pulmonary disease. A focus of bronchopneumonia no larger than the tip of the little finger may prove a vigorous enough centre for the spread of an infection that may express itself loudest, for the reasons given, in terms of cardiac distress. The nerve and muscle cells and fibers of the myocardium are being attacked by the toxin, and the rapid and irregular respiratory movements are coincidently depriving the heart of its supply of blood. Its complaint can be heard and felt throughout the entire economy.

Our first step, therefore, is directed toward the exclusion of primary pulmonary disease.

Next in order of the important causes of secondary cardiac disabilities will be the mischief-making due to gastro-intestinal toxins. These may arise from the decomposition of an oversupply of food or make their appearance in the form of food end-products. Eustis[2] has suggested certain of the amino-acids, especially histamin, as influential in this direction. I have no doubt he is correct in his belief. But long before Eustis or any other medical writer recorded his observations the human individual, lay and medical, was experiencing, with full knowledge of the cause, the hypertension, tachycardia, palpitation, arrhythmia, and precordial pain as the result of an overindulgence in any and every kind of food, and, in the case of certain individuals, of the most sparing indulgence in certain non-protein articles of diet rated as uniformly beneficial. I have had many an uncomfortable personal experience of this kind in the form of a toxemia, many of the expressions of which were purely cardiac and circulatory, resulting from the ingestion of an apple or an orange. An identical picture could and can be produced at any time by shell-fish or by an excess of any kind of food.

Appendicitis, acute or chronic, gastric disorders, duodenal ulcer, simple or tuberculous enteritis, the amebic infections, all spell toxemia and consequent myocardial involvement. Frequently there is added a mechanical factor in the form of tympanites to still further embarrass the involved heart. Not infrequently also there appear acute renal or pulmonary contributions, which, in their turn, burden the heart as it runs the gauntlet of this vicious circle. I have more than once had referred to me a patient with a supposed cardiac disease, whose circulatory symptoms disappeared as soon as the gastro-intestinal tract and the dietary had been subjected to the appropriate hygienic regime.

It is tempting to include the thyroid and pituitary disorders as well as the adrenal affections, and to indicate the prominence and frequency of the secondary reflections in the heart. The grave anemias, the onset of the acute infectious diseases, sepsis in any and all of its forms, may furnish pictures of an essentially cardiac hue.

The point to be emphasized here is that a heart free from antecedent disease may protest so vigorously concerning its vicarious distress as to divert attention from the true etiology and from the seat of primary involvement. It may also invite treatment that will not only prove unavailing, but detrimental, because directed at an innocent, even though a noisy and complaining target.

The second method of discrimination requires equal nicety of judgment, and precision, and thoroughness in the physical examination—namely, the weighing of the influence of a known organic cardiac disease against the secondary symptoms due to incompetency of other organs. All insufficiencies of the lungs, liver, kidneys, or gastro-intestinal tract directly dependent upon cardiac disease are properly a part of the primary cardiac picture, and should be included therein. But we must sharply differentiate between the symptoms attributable to an old valvular lesion with its accompanying myocardial degeneration and those, for example, of an intercurrent infectious pneumonia; we must distinguish between the syndromes of a rheumatic endocarditis and myocarditis and the cardiac symptoms of an intercurrent gonorrhea; and, finally, we must distribute the responsibility for symptoms in the not infrequent coincidence of a persistent influenzal pneumonitis or apical tuberculosis and "rheumatic" or syphilitic organic cardiac disease. The foregoing constitute practical illustrations of the difficulty, as well as the intense interest, involved in the study of the heart in its many relations, primary and secondary.

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[2] New Orleans Med. and Surg. Jour., 1914, p. 730.

It will be of advantage to remember that tachycardia, arrhythmia, cough, blood-spitting, and even the physical signs of acute dilatation may result from pulmonary or gastro-intestinal disease in the complete absence of primary cardiac disease. Demonstrable extension of the right, left, and upper cardiac boundaries, an extended precordial impulse, a muffling of the cardiac sounds, edema of the extremities and of the genitalia, and of the serous cavities, extreme degrees of cyanosis, precordial aching and oppression (as contrasted with sharp pain), and a markedly low systolic blood-pressure, all point to primary cardiac incompetency, both in the presence and absence of contributory symptoms originating in other organs. A high degree of arteriosclerosis in child or adult speaks, *a priori*, for an incompetent heart muscle of long standing. In the child it usually also represents a systemic hereditary syphilis. Such a paper as this might be extended indefinitely. Its value or uselessness will depend upon its success in imbuing the hearer or reader with the need of humble, painstaking care rather than haste in the final determination of the causal factor. Brilliancy, after all, should be only lightning thoroughness.

Careful history-taking is an absolute essential which merits more serious comment than is permitted by the time in hand. The study of the blood-pressure, especially with respect to excessive pulse-pressure or cardiac overload, will often enable one to avoid the error of misinterpreting an organic myocardial disease. An insistence upon the opportunity of eating at table with the patient, and keeping him or her under direct observation during several meals, will occasionally furnish the final clue, uniting and correlating the obscure train of evidently toxemic cardiac complaints.

A blood culture even in an incipient tuberculosis[3] will often afford valuable evidence of the activating factor in a disturbing cardiac syndrome.

I have said enough to attract attention to the importance not only of the ever-increasing number of instances of cardiac and cardiovascular disease, but equally to the vital necessity of separating the physical signs and symptoms that are not primarily due to cardiac disease from those that are.

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[3] Lopatin, Russky Vratch, June 6, 1914. Nine out of sixteen guinea-pigs inoculated gave a positive tuberculosis test.

We must, by every rational endeavor, avoid laying upon the heart an etiological overload in the form of secondary symptoms.

THE CAUSES OF BACKWARD DISPLACEMENT OF THE UTERUS.

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The varied symptom-complex of real or fancied injuries sustained by a railroad, trolley, or traffic accident often presents some reference to the condition of the pelvic organs, and in an examination of the pelvis in an attempt to locate the seat of the trouble a retrodisplaced uterus may be found. That such a condition may occur through an accident seems firmly fixed in the public mind, and even among the profession the idea that sudden or acute retrodisplacement of the uterus can occur through falls, straining or similar injuries apparently finds credence. So by the patient, and not infrequently by the medical attendant, the newly discovered retrodisplacement is held as the cause of the backaches, headaches, and other manifestations of the nervous breakdown or neurasthenia which often follows such an accident. With the idea of such an etiological factor for the condition, legal action to recover damages is instituted against some common carrier, railroad, or trolley line on which at a previous time the patient may have been thrown from her seat or suffered a fall from derailment or other mishap.

The question arises as to whether such a condition as acute retrodisplacement of the uterus may be produced by a sudden fall, strain, or injury. A reference to the standard text-books on diseases of women shows that while such a cause is not considered by some authors, it is mentioned by others simply to deny their belief in it, and where it is classed as a possible factor, it must be regarded as occurring only in extremely rare instances. As a rule, simple retrodisplacement of the uterus *per se* seldom if ever causes symptoms for which medical relief is sought, the accompanying pathology in most cases being responsible for the subjective symptoms. It is possible that a partially retroverted uterus or a uterus already in retroversion might by some sudden increase in pressure of the abdominal contents, as by straining or violent injury, be forced down in the pelvic cavity. In such an instance the sudden ligamentary strain might cause immediate pelvic pain. But in many cases the pain referred to the pelvis is of muscular origin, and has nothing whatever to do with a displaced uterus. The patient previously ignorant of this condition may have noticed no symptoms resulting therefrom, but her attention will remain focussed upon it long after the real effects of the injury have passed away. It would seem that under conditions of normal tonicity the supporting ligaments of the uterus, accustomed to the actively physical life of the average woman, would hardly permit overstretching enough to allow a complete retrodisplacement of the uterus to occur.

There are many factors which influence the production of displacements of the uterus. The one most frequently noted is childbirth, with the accompanying trauma to the pelvic floor and pelvic diaphragm, the early rising after labor, with a subinvoluted uterus illy supported by the imperfectly restored ligaments, or on the other hand, the long dorsal decubitus favoring by gravity the backward displacement of the heavy uterus. Premature interruption of pregnancy, abortions, and miscarriages, so lightly considered by many as to the after-care, predispose in the same manner as labor at term. So in any claim as to the production of a retrodisplacement of the uterus through injury, the nature of any previous pregnancies, their mode of termination, and the attention received in the puerperium would be information of the highest importance.

So, too, any previous disease of the pelvis, infections, or tumors of the adnexa, and pelvic peritoneum with their resulting adhesions, changes in tone or structure of the supporting ligaments, the possibility of a metritis through contiguity, and a consequent weakening of the uterine structure through relaxation or atrophy, and tumors of the body of the uterus, may all cause retrodisplacements passing unnoticed for many months, and whose occurrence in the history of a claimant must be noted.

Congenital displacements often cause no symptoms until perhaps at puberty, when with the onset of menstruation various abnormal phenomena may occur. Or this function may be established normally and, after marriage, sterility often occasioned by the congenital retrodisplacement with its accompanying defects, acute anteflexion, shortening of the vaginal walls, and elongated and stenosed infantile cervix may lead to the first recognition of its presence. But if just previously to or about the time medical attention was required the patient suffered an accident resulting in a severe jar to the body or a fall, it will receive considerable attention as to the part it may have played in being responsible for the symptoms noted.

In order to ascertain to what extent a history of trauma in one form or other occurs in the average case of displaced uterus, I have, through the courtesy of Dr. B. C. Hirst, examined the histories of 529 cases of this condition occurring in his private practice. A number of these cases, referred for pelvic examination as an aid in explanation of some obscure medical condition, represent accidentally discovered cases of symptomless retroposition. Childbirth at term, associated or not, with miscarriage, explains clearly the etiology of a group of 304 cases. In a similar way we can ascribe a previous miscarriage or miscarriages as causing the condition in a second group of 33 cases. The diagnosis of pregnancy or the abnormal symptoms resulting from pregnancy in a retrodisplaced uterus explains the discovery of the displacement in a group of 16 women. There remain two groups, one of 81 sterile married women, and a final one of 88 single women. The total number, 169, of these two groups seems rather high when one considers that childbirth is given as the most common etiological factor by most authorities. In but few of these cases of single or sterile married women was there a simple mobile retroplaced uterus. Some additional pelvic pathology, inflammatory disease of the adnexa, recent or old, and with adhesions, evidences of previous pelvic peritonitis, cystitis, appendicitis, and so on was usually present.

In 13 cases, slightly over 2 per cent. of the whole number of cases, a history of accident or trauma was found. In the first instance the patient had suffered a fractured hip by being thrown from a carriage several years previous to the pelvic examination, which was requested on account of dysmenorrhea and leucorrhea. As this condition followed a period of normal menstruation of four years after the carriage accident, and as she had been informed while undergoing treatment in another city that no displacement existed, it must seem impossible that the accident played any part in the production of this displacement. In the second case a single woman, aged twenty-eight years, menstruation began at twelve years of age. At this time she suffered a fall and was said to have injured her coccyx; for this injury she stayed in bed six weeks. She complained chiefly of pains in the lower abdomen resembling menstrual cramps, which she said followed a second fall received a month previous to the examination. A complete retroversion was found. It would be difficult to say which, if either, of the falls was responsible for the present condition. The third case, a single woman, had a fall or injury in a gymnasium ten years before the pelvic examination. Six years previously her cervix uteri had been dilated to relieve dysmenorrhea, and a pelvic peritonitis developed from which she nearly died. The infection subsequent to the injury would be the most logical explanation for the adherent retroversion. The fourth case was a married woman who a few months before had a miscarriage at two and a half months, occasioned according to her history by a fall down stairs. Her chief complaint was exhaustion, although there was some first-day menstrual pain. She had an apical tuberculous lesion and poor cardiac musculature. These two medical conditions would, no doubt, be more at fault in producing her general weakness than the retrodisplaced uterus found on pelvic examination, and for which she blamed the fall. The fifth case was a married woman who, four years previous to the pelvic examination, during her first year of married life had a miscarriage at three months. Three years later she fell across a chair. Her menstrual history was normal until three months before the examination, when she developed metrorrhagia. She had a bearing-down feeling and complained of pain on defecation. Examination revealed a fissure in ano, marked pain over the appendix, a large cervical polyp, and a retroversion. As polypi are so frequently the result of retained secundines, especially following abortions, the retroversion was much more likely to have been the result of the premature interruption of the pregnancy with the admittedly poor after-care than the minor accident of falling over a chair. In the sixth case the woman fell astride a chair with the development of abscesses, which required incision. This is the history of trauma in a woman whose retrodisplaced uterus was accompanied by pain in the ovaries and metrorrhagia. The history here is too scant to judge what merit the fall might have had in producing the displacement. The seventh patient had a fall fifteen years before the pelvic examination, but the symptoms pointing to the displaced uterus only appeared after a miscarriage a few months previously. The recent miscarriage in this instance is much more likely to have been the cause than the injury sustained so long before. The eighth case, a woman married eight years, had her first pregnancy interrupted, according to her history, by a fall the nature of which is not specified. She dated her chief complaint of pain in the side to a second fall four months before the examination. She had appendicitis, a floating right kidney, and a displaced uterus. While the first fall may have caused the miscarriage, it is just as likely that the uterus was left in a retroverted position after the miscarriage, and that the symptoms of the total pelvic pathology were aggravated enough by the second fall to necessitate a pelvic examination by which the displacement was found. The ninth case, a single woman, dated her trouble, leucorrhea and pelvic discomfort to excessive horseback-riding seven years before the examination. It might be possible that the pelvic viscera and the supporting ligaments would permit a displacement through a long-continued strain as indicated in the history. The tenth case, a single woman, complained of pain along the sciatic nerve, not affected by menstruation, and some irritation of the vulva. The symptoms were stated by the patient to have been apparently started by a fall, and aggravated by another fall. Examination disclosed an anteflexed and retroposed uterus of an infantile type. The condition of the uterus is that most commonly found in cases of congenital retrodisplacement, and it is just as likely that this was the original condition as that it was caused by the fall. The eleventh case was a single woman who dated her chief complaint of leucorrhea from a fall two years earlier. She had severe menstrual cramps after the fall and pain on the right side of the abdomen. Examination revealed a thickening in the base of the right broad ligament and the uterus halfway over. Here the fall probably had less to do with the uterine condition than the inflammatory condition alongside it. The twelfth case, a single woman, complaining of dysmenorrhea, leucorrhea, and backache from puberty, did not have her symptoms affected for the worse by a fall down three stairs a short time before the examination, and which resulted in a severe sprain of an ankle- and knee-joint.

The thirteenth case, a single woman, likewise complained of dysmenorrhea and backache from puberty eleven years before. She had no increase in the severity of the symptoms as a result of a fall from a carriage five years before the pelvic examination revealed the presence of a retrodisplaced uterus.

It is seen, therefore, from a study of these few cases how small and uncertain extent such injuries as falls and strains can be considered as a cause of uterine displacements. It is true that an occasional case is reported in the literature where a uterus found in perfect position a short time before an injury was sustained has been found retrodisplaced on examination made immediately afterward. The suspicion must arise that some accompanying pelvic lesion existed or an examination would hardly have been sought before the fall.

It should be necessary in a legal action to recover damages to show that the patient had been healthy and physically able, and that the uterus was in a normal anteflexed position before the accident. As has been shown above, some women have apparently perfect health and are physically able, and yet whose displacement may only have been noticed after marriage on account of sterility; it would seem difficult to prove satisfactorily that the uterus could have been in normal position without a previous examination. The nature of the accident would have to be considered as to the manner in which it could produce the retrodisplacement of a previously normal uterus. It is possible to conceive, as above stated, that a partially retroverted uterus could by a hard fall on the back or buttocks be converted into a completely retroverted uterus, but it is equally inconceivable that a fall forward on the face or side could be able to produce any such displacement. Insofar as the subjective symptoms are concerned it is seen that few if any symptoms are produced by a simple retrodisplacement. It should be necessary to have proved that immediately after the accident a retrodisplacement did exist. But although after such an accident a retrodisplacement was discovered, this fact would in itself be no evidence that a displacement had not existed previously, even though no symptoms were manifested by it. That retroversion may be caused by trauma is possible, but it is apparent, from the facts stated above, that traumatic retrodisplacement of the uterus is very rare; and that unless it can be shown that the uterus was in normal position just before the accident or injury, it is impossible to prove that the displacement had a traumatic origin.

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CERTAIN UNCLASSIFIED FEVERS: THE TYPHACEÆ (TYPHOID GROUP) AND ENTERICOID OR PARAENTERIC FEVER.

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By unclassified fevers I understand certain forms of infectious fevers which, though frequently met with, and, in part, at least, well known to clinicians in a general way, have not as yet been definitely named. This is due to the fact that often they are passed over as unimportant, and have therefore not been subjected to an exhaustive bacteriological study. Perhaps the main reason why they have not been differentiated is, that our present methods of investigation—bacteriological, chemical, and otherwise—are not far enough advanced to enable us to classify these fevers nosologically.

The fevers under discussion are primarily caused by infective agents, as distinguished from those fevers which are due to disturbances of the function or of metabolism. This latter group may be designated as the fevers of endogenic origin. Menstrual fever may be cited as an example of this type.

The fevers under discussion are also distinct from the fevers of exogenic, chemical origin. Finkelstein's resorption fever after sugar installation in infants is an example of this type. What is generally called gastro-intestinal auto-intoxication is a chapter by itself, the import of which is still *sub judice.* If auto-intoxication causes fever at all it is, in a given case, very difficult to state what part, or how much of the fever, is due to the absorption of the toxic products from the surface of the gastro-intestinal tract, and how much is due to the accompanying bacteremia. What is now popularly called ptomain poisoning, comes under this heading. It is probably nothing more than a gastro-enteritis of bacterial origin. The fevers caused by group A of the paratyphoid bacilli are often accompanied by an acute gastro-enteritis. This is one form of paratyphoid A infection. Both paratyphoid A and B infections, however, may present the complete clinical pictures of typhoid fever. The enteritis of the first form is the result of surface infection. The typhoidal symptoms of the second form are the result of blood-invasion of the paratyphoid bacilli.

Out of the large number of unclassified fevers, I will confine my remarks to a number of those which resemble typhoid fever. Since I have begun to study these cases my attention is not infrequently directed in hospital service toward a form of fever which is brought in, because the patient arouses the suspicion of having a typhoid infection. These cases have the general clinical aspect of that disease. In their future course, they may or may not develop into a genuine case of typhoid fever, as the saying goes. More often, they defervesce in a week or ten days. I am not inclined to think that these cases are abortive cases of typhoid fever. In private practice the occurrence of these typhoid-like fevers are a source of anxiety to the family. A positive answer as to the nature of the illness which is demanded for hygienic and prognostic reasons can often not be given.

The course of this fever resembles that of a mild infection; it comes nearer to the descending curve of the third week of a mild typhoid fever than anything else. Blood cultures are negative. The blood count shows leukopenia or moderate leukocytosis. Eosinophiles are often absent. Relative lymphocytosis may be present or absent. There is no predominating symptom present, pointing to any of the organs. Persistent search for catarrhal symptoms in the respiratory organs is mostly fruitless. In the lack of symptoms—intestinal, respiratory, and otherwise—in the general prostration, the marked enlargement of the spleen—I have palpated the spleen in several instances—in the configuration of the fever curve these fevers strikingly resemble a mild or abortive case of typhoid fever. It must be admitted that these fevers are possibly cases of so-called auto-intoxication. Still, it is difficult to prove them as such, as the decomposition products in the urine, in the shape of the aromatic bodies, scatol, phenol, and indol, are missing.

Judging by analogy, we are dealing here with a mild bacteremia not unlike a typhoid infection. The infective agent in all probability enters the blood through the portals of the respiratory or intestinal lymphatic system. This can only be proved by positive blood cultures which, so far, have not been realized.

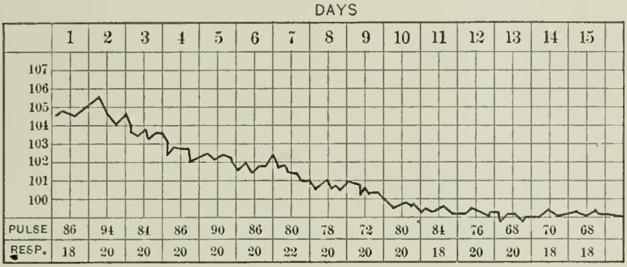

Chart I.—Entericoid or paraenteric fever. Blood count on the third day of the fever: lymphocytes, 28 per cent.; polynuclears, 60 per cent.; large mononuclears, 10 per cent.; eosinophiles, 1.5 per cent. Widal and Diazo negative throughout. Agglutination against six paratyphoid strains negative.

Those of us who practised during the great influenza pandemics of the late eighties and early nineties, observed cases of group-infections of influenza in families, some of which strikingly resembled typhoid fever. Since that time I observe every year a number of cases of fever, typhoid-like in character, which go under the name of influenza, but which are not caused by the influenza bacillus of Pfeiffer, as proved by negative sputum culture, in appropriate media, but are due to infection with pneumococci or streptococci.

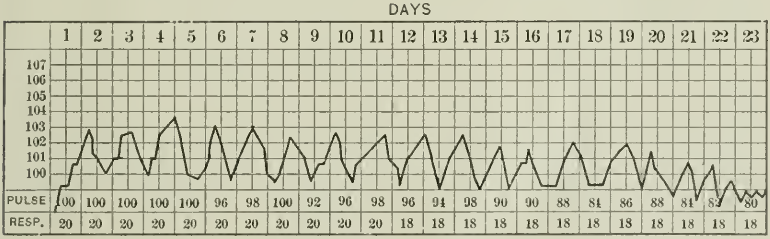

Chart II.—Entericoid or paraenteric fever. Blood count on the second day: reds, 4,328,000; leukocytes, 12,200; small mononuclears, 10 per cent.; large mononuclears, 9.5 per cent.; polymorphonuclears, 79 per cent.; eosinophiles, 1.5 per cent. Blood count on the fifteenth day: reds, 3,853,000; leukocytes, 13,500; small mononuclears, 24.6 per cent.; large mononuclears, 13 per cent.; polymorphonuclears, 59 per cent.; eosinophiles, 3.4 per cent. Widal reaction negative up to 1 : 100. Diazo negative. Agglutination against six paratyphoid strains negative.

These fevers may start in with catarrhal respiratory signs. If they do not, they are often unmasked late in the disease by resolving into a predominant general bronchitis.

In an interesting contribution by Dr. David Riesman of Philadelphia, discussed by Dr. Hobart Amory Hare,[1] it is proposed to call the fevers allied to the typhoid fevers, entericoid fevers, febris entericoides. I have called them typhocoid or paranteric fevers. Presumably these fevers are caused by the bacteria closely allied to the bacillus of Eberth. Since Schottmüller's description of the paratyphoid groups A and B, a dozen or more observers have added distinct varieties of this group which are known by the names of the discoverers. Typhoid-like fevers may also be caused by the paracolon bacilli. Warren Coleman[2] described a case clinically identical with typhoid fever, inclusive of rose spots, caused by a colon bacillus. Schottmüller[3] recently described an epidemic of herpetic fever in women, which was associated with urinary symptoms. The pus in the (oral) labial herpes contained a pure culture of a colon bacillus.

Someone has said that Escherich's discovery of the colon bacillus was hailed as an unwelcome event in bacteriology, as innumerable questions, serological and otherwise, were raised by the seemingly inexhaustible number of strains of the colon bacillus; the answers to most of these questions have so far been unsatisfactory, especially has this been so as regards the subject under discussion. Perhaps some day will be written the biological history of the ascendency of the colon bacillus into the fixed types of the various forms of typhoid fever.

It might not unjustly be said, that the foregoing observations on the interpretation of these unclassified fevers have, after all, only a theoretical or at most, a purely scientific significance, were it not for the fact, that in a number of instances, I have seen mild fevers of this kind, after a short subsidence, merge into severe cases of typhoid fever. Now there can be no doubt that in these instances these initial febrile movements which are seemingly identical with the entericoid or paraenteric fevers described above, constitute the introductory stage of true typhoid fever. We must assume that after the usual low temperature fluctuations of the incubation stage of typhoid fever is passed, there is a preliminary or initial fever, in these cases of typhoid fever of a week's, ten days, or fortnight's duration. Sometimes this initial fever is apparently nothing else than a primary access in irregular, atypical forms of typhoid fever. The complete *ensemble* of the case then shows a series of such accesses with remissions. It lies in the nature of the case, that the initial stages of typhoid fever have not been subjected to the careful observations of the later stages. In the large number of cases, at least in hospital practice, the patient does not come under observation before the second or third week of the fever, or even later. I have at present a case under observation, which presented this initial stage. At that time the patient showed a large spleen with a mild febrile movement. Diazo reaction negative. After a short remission, rapid rise of temperature, spleen larger, diazo strongly positive, blood-culture negative. Numerous rose spots. Moderate leukocytosis, eosinophiles constantly present. Widal reaction, taken every few days, absolutely negative. In the sixth week, Widal positive, 1 to 20. It has been negative ever since. Reaction against all available paratyphoid strains negative. Culture of urine and feces negative. Complement-fixation for typhoid fever negative. The steady increase in hemoglobin and eosinophiles and the slow but certain reduction in the size of the spleen in this, the eighth week, seems to prove that complete convalescence has already set in.

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[1] Jour. Amer. Med. Assoc., December 29, 1913, p. 2205.

[2] Amer. Jour. Med. Sci., 1909, cxxxviii, 198.

[3] Beiträge z. Klinik d. Infectionskrankheiten, vol. i, No. 1.

From what has been stated it becomes evident that the fevers under discussion will bear close study. In a given case, the question to be decided is, Am I dealing with a case of typhoid fever or not? This is often decided soon enough, when unmistakable clinical evidence is present. The laboratory corroborates the diagnosis sooner or later. If the diagnosis of typhoid fever cannot definitely be made, the situation is a puzzling one. We have seen that there is a class of fevers, clinically resembling typhoid fever, which at present it is hard to classify, and to give a distinctive name. No doubt we are dealing with infections of various kinds. Their true nature will not be determined until they are subjected to an exhaustive biological research.

Furthermore, there is a class of fevers which clinically are unmistakably typhoid fevers, but in which, also, the laboratory proof is inadequate. This opens up the large question of the biology of the typhaceæ. This name has been used by Loeffler[4] to designate the colon, paracolon, paratyphoid, and typhoid groups of bacteria. The same name, I think, may also be used as a collective appellation for the various groups of fevers caused by these typhoidogenetic bacteria. Typhoid fever, a clinical entity, is produced by a variety of infective agents. Some of these have been determined; their biological reactions are well known. Others are still to be isolated. A comprehensive study of the bacteriological relationships of the typhaceæ fevers among themselves, the determination of the appropriate culture media for each variety of bacteria, the amplification of our knowledge of agglutination, complement-fixation, opsonic index and other biological reactions will serve to classify the individual case in the clinic.

For valuable assistance in the laboratory, I am indebted to Drs. Hensel and Garbat.

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[4] XIV International Congress for Hygiene and Demography, 1907, and Weber and Haendel, XV International Congress for Hygiene and Demography, 1912.

REVIEWS

A Practical Treatise on Diseases of the Skin. By Oliver S. Ormsby, M.D., Professor and Head of the Department of Skin and Venereal Diseases, Rush Medical College (in Affiliation with the University of Chicago); Dermatologist to the Presbyterian, Children's Memorial, Saint Anthony's, and West Suburban Hospitals, The Home for Destitute Crippled Children, and The Orphan Asylum of the City of Chicago; Member of The American Dermatological Association and of the Congress of American Physicians and Surgeons. Pp. 1168; 303 engravings and 39 plates in colors and monochrome. Philadelphia and New York: Lea & Febiger, 1915.

The writer first gives a detailed account of the anatomy and physiology of the skin, general symptomatology, etiology, pathology, diagnosis, prognosis, and therapeutics. The diseases of the skin, for the purposes of study, are divided into nine classes: hyperemias and inflammations; hemorrhages; hypertrophies, atrophies; pigment anomalies; new growths; neuroses; parasitic affections, subdivided into diseases due to vegetable parasites and diseases due to animal parasites; diseases of the appendages, subdivided into diseases of the sweat glands, sebaceous glands, hair and hair-follicles, nails, and mucous membranes. This classification is practically the same as used by Hyde, with the exception that the term neuroses is substituted for sensory dermatoneuroses and the group "Diseases of the tropics and warm countries exhibiting cutaneous lesions" is omitted.

The writer speaks authoritatively of pellagra; as Secretary of the Illinois Pellagra Commission, he had a considerable opportunity of studying this important disease; several excellent photographs are given. Thirty pages are devoted to the exanthemata which enhances the value of the present volume. The Wassermann and luetin tests are given in detail, including their value in syphilis. The therapeutic indications and the exact method of employing salvarsan and neosalvarsan are presented. The term xanthelasma is used for eyelid xanthoma, as suggested by Pollitzer and adopted by the American Dermatological Association. The classification of syphilis, as suggested by George Henry Fox is mentioned but not employed in the present volume. The important subject of leukemia cutis is given in considerable detail, which is a great advance over most of the recent works on dermatology. The general subject of trichophytosis is brought up to date by the inclusion of several photographs of plate cultures showing the ringworm fungus. The pathological description of the various dermatoses is fully and clearly given and numerous photomicrographs help in the elucidation of the text. The author has drawn largely from his own collection of photographs, those from the former edition of Hyde's treatise and from his many friends, thereby giving his volume the aspect of an atlas in addition to the valuable reading mater. All of the common and most of the unusual cutaneous affections are depicted in either black and white or color. The book is an important addition to the dermatological field. If any criticism could be offered, the reviewer would state that the present volume is practically a revision of Hyde's *Diseases of the Skin.* A revision which makes the latter volume complete with all of the many advances in the dermatological field. F. C. K.

PATHOGENIC MICROÖRGANISMS: A PRACTICAL MANUAL FOR STUDENTS, PHYSICIANS AND HEALTH OFFICERS. BY WILLIAM H. PARK, M.D., Professor of Bacteriology and Hygiene in the University and Bellevue Hospital Medical College, and Director of the Bureau of Laboratories of the Department of Health, New York City, and ANNA W. WILLIAMS, M.D., Assistant Director of the Bureau of Laboratories, New York City; Consulting Pathologist to the New York Infirmary for Women and Children. New (5th) edition, thoroughly revised. Pp. 684; 210 illustrations and 9 full-page plates. Philadelphia and New York: Lea & Febiger.

THE fifth edition of this valuable manual appears, after a four-year interval, with 18 more pages and 14 more engravings and 9 full-page plates instead of 8. Only one of these, however, is the same in the second edition. Especially noteworthy are Williams' drawings of protozoa and Negri bodies.

Under a new arrangement of material, Part I deals with Principles of Microbiology; Part II, Pathogenic Microörganisms Individually Considered; Part III, Applied Microbiology. This last part, a development of three chapters scattered through the previous editions takes up the relations of milk, water, air, soil, and sewage to disease, bacteriological methods of examination of the same, and practical disinfection and sterilization.

It is pleasant to note the "up-to-date" treatment of trachoma and rabies, Cole's differentiation of four types of pneumococci, and of Mallory's recent studies in pertussis. Noguchi's growth of the rabies organism on artificial cultures is not corroborated; one regrets that space has not also been found for treatment of Gay and Claypoole's work on *Streptothrices*.

The index is full and conveniently preceded by an author's index. The book is of great value to medical students, both graduate and undergraduate. E. B. K.

Text-book of Surgical Operations Illustrated by Clinical Observations. For Physicians and Students. By Prof. Fedor Krause, Privy Medical Councillor, Directing Physician Augusta Hospital, Berlin, in association with Emil Heymann, M.D., Chief Physician, Augusta Hospital. Translated and Edited by Albert Ehrenfried, A.B., M.D., F.A.C.S., Assistant Visiting Surgeon, Boston City Hospital; Assistant in Surgery, Harvard Graduate School. Vol., 1; pp., 267; 55 plates having 233 colored illustrations, 61 figures in text. New York: Rebman Company, 1915.

By being the first to excise the Gasserian ganglion, in 1893, Prof. Fedor Krause ranks with the immortal German surgeons of the nineteenth century who originated operations, and is the worthy successor at the Augusta Hospital of another of this small group of five, Ernst Kuester. In his own words: "The purpose of the book consists in this, that it offers to every properly trained physician a foundation upon which he can independently undertake the operations described. In order to fulfil this purpose in all its details, pictures true to nature explaining the different phases of each operation have been liberally supplied on special plates." And in the words of the translator: "This book is, primarily, a text-book of operative surgery. It approaches its subject in a novel way, by the presentation and discussion of actual cases, which are carefully followed from the beginning, through the operative treatment, to the end-result. These cases illuminate the text and give a touch of practical interest to what might otherwise be a dry discussion. This is, in fact, an application of the case-teaching method to surgery." Perusal of the volume bears out these statements completely.

The twelve chapters cover general surgical technique and operations upon the head. The first four chapters, occupying the first seventy-nine pages, and covering the grounds of preparation for operation, anesthesia, asepsis and after-treatment, might have been omitted with advantage, as they are not germane to the scope of the book, and are so elementary that one who has not already mastered them in the days of his internship had better not attempt to perform the operations that follow. Furthermore, German technique differs in many respects from American, and it seems useless to complicate matters.

A few minor criticisms of details, throughout the book might be made. Most of us would find it very difficult to "tie every spurting vessel" of the scalp. We agree that every accidental wound of the scalp should be considered septic, and explored for injury to the skull. We do not agree that "excellent results may be obtained with scarlet red or fuchsin ointments." Radium should be recommended for hemangioma of the face. The conjunctiva cannot be spoken of as "mucous membrane," for it, as well as the lining of the prepuce and covering of the glans, is modified skin (ectoblast). Unfortunately, the fallacy of referring to lymph nodes as lymph glands is made in this work. In carcinoma of the lip it is advised to ablate cancerous lymph nodes after the extirpation of the lesion. For obvious reasons we consider it better technique to reverse this order. It is easier and less traumatizing to remove the outer wall of the orbit with the Gigli or motor saw than with the chisel. In children the mastoid cells are not developed, but this is not brought out in the book. The suprameatal triangle, the guide to the antrum, should bear MacEwen's name. In Schloffer's method of exposing the sphenoidal sinus and the hypophysis the following direction is given: "After a small sagittal incision was made with a knife in the middle line 56 cm. behind the bony root of the nose." This sentence should continue: "the undertaker should be summoned." Of course, 56 mm. is meant. It is not clear how the frontal nerve can be exposed without cutting through the periosteum of the roof of the orbit, for it lies under cover of that membrane. Blocking of the lingual nerve within the mouth should be performed instead of resection. After excision of the second and third divisions of the fifth nerve, Kanavel's method of plugging the foramina with bone-pegs receives no mention.

The arrangement of the book is ideal in that almost every technical detail is illustrated, leaving nothing to the imagination of the reader. The illustrations are copious—even lavish—and of artistic merit. The translation is so well done that one could scarcely believe the book had been written in another language.

If the remaining volumes fulfil the promises of the first, we would say that the ideal work on operative surgery has appeared at last.

P. G. S., Jr.

Cancer: its Cause and Treatment. By L. Duncan Bulkley, M.D., Senior Physician to the New York Skin and Cancer Hospital. Pp. 230. New York: Paul B. Hoeber, 1915.

Bulkley endeavors to prove in his small volume that the eradication of cancer depends largely, if not wholly, upon proper metabolism. The metabolic process being entirely correct if the character of the food ingested is restricted to certain articles and the kidneys and bowels are either normal or have an increased activity. The writer states that to prevent the occurrence or recurrence of cancer, it is absolutely necessary to maintain a perfect vegetarian diet, which includes even the exclusion of eggs and milk from the food. The distribution of cancer is governed by the diet; those races indulging largely in meat are very prone to the tumor formation, while those partaking exclusively of a vegetarian or rice diet are comparatively free from the disease.

According to Bulkley, "there have been plenty of good men who knew the disease and have reported favorable results, and even complete disappearance of cancer, under dietetic regimen and proper medication alone, without operative interference of any kind." Several cases of cancer of the breast, with lymphatic gland enlargement, are cited which entirely recovered under vegetarian or rice diet and the free flushing of the intestinal and urinary tracts. The millennium insofar as the cure and prevention of cancer, has come if we all could only obtain the results of the writer of the attractive and readable volume under discussion. F. C. K.

Pyelography (Pyelo-ureterography). A Study of the Normal and Pathological Anatomy of the Renal Pelvis and Ureter. By William F. Braasch, M.D., Mayo Clinic, Rochester, Minnesota. Containing 296 Pyelograms. Philadelphia and London: W. B. Saunders Company, 1915.

To Braasch more than any man in this country belongs the credit of demonstrating the value of pyelography in the diagnosis of surgical diseases of the kidney. As the result of his large experience and careful observations, he is especially fitted for the preparation of this excellent monograph which takes up every phase of the subject, including an exhaustive survey of the literature. The opening chapters contain a *resume* of the history of pyelography together with the accidents that may follow collargol injection. The author is of the opinion that these ill results are in the majority of instances attributable to faulty technic or improper selection of cases. He states that pyelography has proved of too great value to allow it to be discarded because of an occasional reaction, but it should be employed only with the strictest precautions and by those who are expert in cystoscopic work. Numerous pyelograms are given illustrating the various types of the normal pelvis and ureter. Accompanying these are detailed descriptions, making the chapter of especial value. The succeeding chapters are devoted to deviations from normal as the result of disease. Both mechanical and inflammatory dilatations of the pelvis are discussed from the standpoints of diagnosis and the types of cases suitable for injections. In cases of renal calculus, pyelography should be employed only when interpretation of the plate is doubtful or when exact localization is desirable. That pyelography is of decided value under such circumstances is nicely shown in numerous plates. The final chapters deal with tumors of the kidney and congenital anomalies in their relation to pelvic distortions, et cetera. We have nothing but praise for this monograph which presents the last word in pyelography. F. E. K.

THE CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Volume IV, Number II (April, 1915). Octavo, 197 pages, 47 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THE present issue of *Murphy's Clinics* opens with a diagnostic talk by Dr. Murphy on osteomyelitis. While this is written in Dr. Murphy's best vein, yet but little is added to what has been covered by four talks in previous numbers.

The next case is one of "Bony Lipping of the Right Acetabular Margin and of the Neck of the Femur Following a Metastatic Arthritis—Arthroplasty of the Hip—Cheilotomy." Subscribers to the *Clinics* must have acquired a fair knowledge of this subject from the eight talks on the hip that have appeared in previous issues. The Roentgenogram presents the appearance of the common hypertrophic osteoarthritis, or morbus coxæ. The operation is termed cheilotomy one place and cheilectomy another.

Dr. Rodman's talk on "Carcinoma of the Breast" is very elucidative. His experience with Paget's disease must have been exceptionally extensive to warrant the phrase, "Nearly all the patients with it that I have seen . . ." His interpretation of the pathology, that it is duct cancer with secondary cutaneous involvement, should be emphasized. He states in italics: "*The muscles are removed not because they are involved in the carcinomatous process*, as so many think, *but simply for the reason that a thorough axillary dissection cannot be made with the muscles in situ*." If this is the only reason, why remove the pectorals at all? Why not reflect them and stitch them back, just as when one deals with the infrahyoid muscles in the removal of a large goitre? Referring to ligation of the superior thoracic artery, Dr. Rodman says: "I have convinced myself by work in the dissecting-room that it is at least a hazardous, if not an unwarranted, procedure." And yet on the very next page, "The superior thoracic, which is about the middle of the upper flap, is seized and ligated."

The fourth case is an inoperable carcinoma of the colon with diffuse miliary "carcinosis" of the peritoneum. A case of carcinoma of the colon was discussed in a previous issue.

The fifth case is one of epithelioma of the upper lip starting in an old lupus scar, for which excision, with plastic closure, was performed. The sixth case is an intramural fibroid of the uterus. The seventh case is one of hypertrophy of the prostrate, complicated; perineal prostatectomy. Much of the ground was covered in two previous talks, one of which appeared in the October, 1914, number.

The eighth and last case, one of spontaneous massive coagulation of cerebrospinal fluid with xanthochromia, was introduced with a diagnostic "talk" by Dr. Mix. This assumed monographic proportions, covering 52 pages, and leaves one in a quandary how Dr. Murphy found any time left to operate that day. It includes abstracts of 33 cases from the French and German literature, with a complete bibliography at the end. Readers of the *Clinics* are more apt to be bored than entertained by this "talk," unless they be neurologists, but Dr. Murphy sums up the essential points in his ensuing comments, which form the most interesting part of this issue. Two excellent illustrations, one in colors, by Tom Jones, are included here.

Boiling the issue down, the faithful subscriber gets very little "new" material. He only gets 8 topics, whereas previous issues have contained from 12 to 21. It seems far better to maintain the freshness of this publication by issuing it quarterly or even semi-annually, than to be forced to the necessity of repetition and obvious padding, in order to issue it bi-monthly.

BERIBERI. By EDWARD B. VEDDER, A.M., M.D., Captain Medical Corps, U. S. Army. Cartwright Prize for 1913. New York: William Wood & Co.

OF great practical as well as scientific worth this book passes the added distinction of being, for a work of this kind, unusually readable.

The story of beriberi from the earliest times to our own, as presented by the author offers an engrossing tale. It will appeal not only to physicians and scientific men in general, but to anyone who can appreciate the story of a tremendous work well done.

One of its most attractive features is the way in which evidence, offered by opponents to the theory of beriberi to which the author holds, is taken and by careful analysis and the verification or disproof of the facts as stated, is shown to support rather than controvert his belief.

The author proves conclusively, that beriberi is caused by a dietary deficiency; that it is a lack in various diets rather than a specific poison or infection in them that is at fault.

The correlation of the beriberi of fowls and animals with human beriberi makes possible the experimental proof of beliefs formed from the observation of beriberi in man.

The only criticism, if such it may be called, is that after driving a truth home and clinching it, the author proceeds to clinch it time and again. This may, at times, weary a reader who has grasped the significance of proofs offered and already formed his conviction.

Practically the beriberi question should be in large part a closed one and the ravages of this dread disease in the Orient and elsewhere (for it is shown to be of almost world-wide distribution) should cease. A. A. H.

TEXT-BOOK OF ANATOMY AND PHYSIOLOGY FOR NURSES. By AMY S. POPE, Instructor in the School of Nursing of the Presbyterian Hospital in the City of New York. Pp. 545; 135 illustrations. New York and London: G. P. Putnam's Sons.

To be able to say how much and how little a text-book on anatomy and physiology should offer to nurses is a difficult problem to solve. The author of this volume exhibits a proper estimate upon the relative importance of the various parts of her subject matter, and presents them in an entertaining and impressive style. Some features of the usual nurses anatomy have been omitted; not however with any consequence.

The portion dealing with physiology is well done. It keeps pace with the growing needs of the nurse as teacher of hygiene and sanitation, together with her increasing opportunities in the social service field.

While the book is rather fully illustrated, it is not unfair to say that some of the pictures could be improved; especially so, inasmuch as a lasting portion of the nurse's idea must come from these illustrations. T. G. S.

DISEASES OF BONES AND JOINTS. By LEONARD W. ELY, M.D., Associate Professor of Surgery, Leland Stanford Junior University. Pp. 218; 212 illustrations. New York: Surgery Publishing Company.

THE author shows a commendable effort toward compactness and to follow broad general principles. In the first chapter anatomy, physiology, and pathology are discussed, but throughout the whole book pathology receives prime consideration and is presented in the light of the most valuable recent contribution to the literature, a considerable bibliography being given. Only 38 pages are devoted to bone diseases and 21 pages to acute joint diseases. The greater part of the book is given up to those chronic affections of joints which are so troublesome to the patient and physician and concerning which there is so much to learn. Brevity and comprehensiveness are attained, chiefly, by restriction to general principle and to the gist of the subject. Instead of having on the top of both opposing pages the title of the book it would be better to have on one the title of the chapter under discussion, particularly as six of the nine chapters do not begin on the page indicated by the list of contents. But this detracts little from the value of the book. T. T. T.

Dental Diseases in Relation to Public Health. By J. Sim Wallace, D.Sc., M.D., L.D.S., Formerly Dental Surgeon and Lecturer on Dental Surgery, London Hospital. Vol. 8., pp. 90. London: Office of the Dental Record.

Beside directing attention to the great prevalence of dental diseases, as well as the seriousness of infections in various parts of the body with the tissues about the teeth as the original foci, the author directs attention to the inter-relationship of food habit and dental caries. He draws attention to the value of a knowledge of the physiology of oral hygiene, especially for medical students, and gives a short but comprehensive treatise upon the same. In closing he describes the results of dental diseases upon the development of children. C. P. S.

Aids to Dental Anatomy and Physiology. By Arthur S. Underwood, M.R.C.S., L.D.S., late Professor of Dental Surgery at King's College, London; Member of the Board of Examiners in Dental Surgery, Royal College of Surgeons of England; Lecturer in Dental Anatomy and Physiology at the Dental Hospital of London. Third edition. Pp. 136. New York: William Wood & Co.

While this little book is concise, it must not be regarded in any sense as a quiz compend or as dealing with essentials only. In fact, it covers thoroughly the whole subject of development, histology, and gross anatomy of the human teeth, together with an insight into comparative dental anatomy. Some of the views expressed by the author upon certain points have not met with general acceptance, notably the alleged demonstration by Mummery of nerve fibers in the dentine. In an appendix is contained Mummery's communication to the Royal Society, which represents the most recent original work upon calcification of dentine and enamel. A few illustrations would have greatly enhanced the value of the book. R. H. I.

PRINCIPLES AND PRACTICE OF HYDROTHERAPY. By GEORGE KNAPP ABBOTT, A.B., M.D., Dean and Professor of Physiologic Therapy and Practice of Medicine in the College of Medical Evangelists, Loma Linda, Cal. Second Edition. Pp. 510; 127 illustrations. Loma Linda, Cal.: The College Press.

GREAT care has been exercised to make this work thoroughly practical, and while explicitly stating the beliefs and explaining the practices of the most advanced hydrotherapists, the book will surely prove acceptable to the most conservative, and presents in an attractive form, much that will be new to the general practitioner.

This work is a concise treatise on the subject which will give the practitioner as well as the hydrotherapist, in few words, systematically arranged and well illustrated, the key to the successful application of these physiological measures. M. J. W.

THE FECES OF CHILDREN AND ADULTS. THEIR EXAMINATION AND DIAGNOSTIC SIGNIFICANCE, WITH INDICATIONS FOR TREATMENT. By P. S. CAMMIDGE, M.D. (London). Pp. 516; 13 full-page plates, 7 of which are colored, and 96 illustrations. New York: William Wood & Co.

THIS work comprises a very complete and thorough exposition of the laboratory examinations of feces, normal and pathological, and all that they may contain. Of particular practical use are the chapters on the diagnostic value of examinations of the feces, in which the fecal findings in a variety of diseases are set forth, and the appendix, which contains a large number of diet lists for gastro-intestinal affections, advocated by various authorities. Another chapter deals with indications for treatment, including a short description of the caloric method of estimating the value of diets, the dietary indications in certain affections, the use of drugs, vaccines, etc. In the main, the advice conforms to orthodox teaching, but the section devoted to infant feeding is far too didactic and condensed to be of much practical use. To attempt to indicate briefly the royal road to success in infant feeding is but to attempt the impossible. To practitioners and students who desire practical as well as technical aid in treatment and diagnosis, the book makes a special appeal. J. C. G.

MECHANICAL VIBRATION. ITS PHYSIOLOGICAL APPLICATION IN THERAPEUTICS. By M. L. H. SNOW, M.D., Professor of Mechanical Vibration Therapy in the New York School of Physical Therapeutics, etc. New York: The Scientific Authors' Publishing Co.

SNOW'S book deals first with the "development of mechanical vibrations" in which in an interesting fashion he begins with the early records and merges through massage principles into his own topic. He devotes but little to vibration apparatus *per se*. Systems of vibration therapy receive brief mention. Method of application is given special emphasis. General physiological effects are accorded prominence, as are also the principles and effects of mechanical vibration in diagnosis. Influences upon the heart, vascular, ductless gland, lymphatic, respiratory, muscular, nervous, and digestive systems are separately discussed. The theme is an admixture of advanced and elementary facts. In the hands of the younger student of the subject, provided his purpose is to place the principles in a worthy position in therapeutics, the book must be of value. Frequent reference is made to persons as authorities in whom the medical profession as yet has not imposed much trust. There is a trend of suggestion throughout the context which leads the reader to think that its author tends to regard his principle as an independent art in therapeutics. However, the work suggests a vast amount of labor, study and application to principles therein discussed; it will probably help many an honest student of this special theme, and should find its proper level in medical literature.

W. J. M.

SCIATICA. A FRESH STUDY. By WILLIAM BRUCE, M.A., LL.D., M.D., DINGWELL, N.B. Pp. 175; 17 plates. New York: William Wood & Company.

THE hypothesis of Bruce who has observed more than a thousand cases is "that the true cause of sciatica is trouble in the hip-joint." He endeavors to discredit Gowers, though the latter states that senile rheumatic inflammation of the hip-joint is a common cause of sciatica, but maintains that the disease in the nerve is essentially a neuritis and as a rule has attacked the muscular and fibrous tissues first. "Granting the presence of this fibrositis" Bruce contends, "it is not easy to see how the condition is likely to spread to the nerve." The inflammation passes along the white fibrous tissue which extends practically throughout the body. As to an actual neuritis in the sciatic nerve, which Bruce doubts, the Danish surgeon, Pars, who stretched the nerve a number of times, found in at least half of the cases that the nerve was abnormally red.

We see no reference to the masterful article contributed by Professor Karl Petrén in 1909. The differentiation there is made between sciatica due to hip-joint trouble and that of other origins.

N. S. Y.

AIDS TO PRACTICAL PHARMACY. By A. CAMPBELL STARK, M.B., B.S. (Lond), L.S.A. (Eng.) Ph. C., University Medallist and Exhibitioner in Materia Medica, St. George's Hospital, Medical School, etc. Second edition; pp. 165. New York: William Wood & Company.

THIS work, based on the British Pharmacopœia, presents in compact form the important facts concerning the different drugs. Its strongest appeal would be to the pharmacist and after him, probably, to the dispensing physician. S. J. R.

RENAL DIAGNOSIS IN MEDICINE AND SURGERY. By DR. VICTOR BLUM, Tutor in Urology at the University of Vienna. English Translation by WILFRED B. CHRISTOPHERSON. Pp. 142. New York: William Wood & Co.

THE immense progress made in renal surgery in the past few years is largely due to advances in our methods of determination of kidney function. It is well recognized that the knowledge derived from these functional tests is essential for the proper management of both surgical and medical conditions of the kidney.

The book begins with a consideration of the particular function of each portion of the kidney as established by experiment. The various methods of determination of renal function are then described in detail. Finally the author takes up the application of the various tests to particular lesions of the kidney. In the author's opinion the following tests afford the most valuable information as to the functioning powers of the kidneys: Cryoscopy of the blood and urine, the indigo-carmine test, experimental polyuria, estimation of urea, and diuretic experiments. He apparently does not measure the percentage of indigo carmine excreted, but only notes the time of onset of excretion of the drug, which he prefers to phenolsulphonephthalein. The use of the various tests is illustrated by many instructive cases of diseased conditions of the kidney and ureters. The literature of the subject is fully reviewed, and the work of a few Americans in this field has been given due recognition. R. H. I.

EPIDEMIC INFANTILE PARALYSIS (HEINE-MEDIN DISEASE). By PROFESSOR PAUL H. ROEMER, Principal of the Institute of Hygiene and Experimental Medicine of Marburg. Translated by H. RIDLEY PRENTICE, M.D., B.S. (Lond.), M.R.C.P.; Late Resident Medical Officer to the National Hospital for the Paralyzed and Epileptic, Queen Square. Pp. 208; 57 illustrations. New York: William Wood & Co.

THIS is a very good translation of Professor Römer's book on *Epidemic Infantile Paralysis*. The basis of this work was the recent epidemic in Marburg which led the author to investigate this disease from the experimental stand-point. The results of his studies have been published elsewhere and finally resulted in this work which is an excellent presentation of the present experimental, pathological, and clinical knowledge of the disease. There is nothing new in the conclusions simply because we have not as yet reached that stage in which conclusions can be arrived at. This book is along the same line as the very excellent book on the same subject by Professor Wickman. T. H. W.

THE PSYCHOPATHOLOGY OF HYSTERIA. By CHARLES D. FOX, M.D. Pp. 437. Boston: Gorham Press.

THIS book is largely made up of the elucidation of symptoms of hysteria from the standpoint of the French and Boston schools. The Freudian points of view are only mentioned, but are not especially considered. The author has carefully presented the subject and made extensive use of the literature, and if one wishes a careful presentation of symptoms of hysteria, this book fulfills that need. T. H. W.

AMBIDEXTERITY AND MENTAL CULTURE. By H. MACNAUGHTON JONES. Pp. 102; 23 illustrations. New York: Rebman Company.

THIS important matter is discussed in a small popular edition. Medical men and teachers do not always appreciate the value of being able to use both hands, for, as is well known, the left side of the brain, because of the preponderant right-handedness of individuals, is much more developed than the right. This should not be, for we should not have a silent area of the brain. In this book the plea is made for the development of both hands in all matters pertaining to them. Dr. Montessori's method is touched upon. This book should be in the hands of all teachers. T. H. W.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Salvarsannatrium.—Wechselmann (*München. med. Wchnschr.*, 1915, lxii, 177) publishes his experiences with about twelve thousand injections of Ehrlich's newest preparation, salvarsannatrium or salvarsan-sodium. This substance possesses all the advantages of salvarsan and neosalvarsan. It is very soluble in water and on exposure to air rapidly becomes toxic. Wechselmann has used the new preparation in doses of 0.3 to 0.45 gm. and has had no reactions following its use in ambulatory and hospital patients. Only twice has he noted morbilliform eruptions. Such doses may be given twice a week and in recent cases, after total dosage of 4 to 6 gm., the clinical symptoms have practically always cleared up, Wassermann reaction has become negative in the serum, and in about 93 per cent. of the cases, the spinal fluid has become negative. The method which Wechselmann has used in giving salvarsannatrium is as follows: The drug is dissolved in 0.4 per cent. sodium chloride solution in proportion of 1 to 100. The salt solution must be prepared from freshly distilled water and chemically pure sodium chloride and is sterilized by boiling in Erlenmeyer flasks. The drug is not added till the solution has cooled. The solution is then filtered through absorbent cotton (Verbandwatte) which has been sterilized by boiling in 0.4 per cent. sodium chloride solution. The flasks, etc., are sterilized by heating to 120° C. In a vast majority of cases, the author has given the drug intravenously.

On the Treatment of Typhoid Fever with Typhoid Vaccine.—H. Eggreth (*Wien. klin. Wchnschr.*, 1915, xxviii, 209) reports the results of forty-eight cases of typhoid fever treated with Besredka's typhoid vaccine, given according to the method of Kraus. First, a subcutaneous injection of vaccine was given. Only a slight local reaction was obtained. Then 0.5 to 1 c.c. of vaccine was given intravenously. Each of the forty-eight patients received only one injection. In thirty-eight cases the result was striking, in eight there was little effect; two patients died. In the thirty-eight cases, the injection was followed almost immediately by slight chill and rise of temperature of 1° to 1½° C. The temperature remained at this higher level, to fall by crisis to normal after six to ten hours. Often there was marked sweating with the crisis. There was never any evidence of cardiac collapse; occasionally there was nausea. In addition to the fall in temperature, there was often improvement in the cerebral symptoms, such as headache, vertigo, stupor, etc. In general, it seemed that the patients who were treated in the first and second weeks of the disease and in whom there were no complications, reacted best. Thirty-four of the thirty-eight cases remained afebrile. In one case, the temperature rose the day after the crisis. In the remaining three cases, the temperature rose on the twelfth, fourteenth and sixteenth day, due to parotitis, osteoperiosteitis and endocarditis respectively; all recovered. The second group of eight cases consisted of patients in the fourth and fifth week of typhoid who were suffering with bronchitis, broncho- or pleuropneumonia. In these there was no critical fall of temperature. All of them recovered, however. In the two fatal cases, death followed about three hours after the intravenous injection. One patient was dyspneic, cyanotic and had râles and dulness in the left back. Autopsy showed, in addition to the usual changes of typhoid fever, a beginning pneumonia, some clear fluid in the pericardium, etc. In the second case, the patient was anemic and fresh blood was found in the ileum. The patients were treated in a military reserve hospital. The diagnosis was confirmed in all cases by positive Widal and diazo reactions. Blood cultures apparently could not be made.

On a New Method of Treatment of Tuberculous Meningitis.—J. Bacigalupo (*München. med. Wchnschr.*, 1915, lxii, 222) reports his observation in three cases of tuberculous meningitis in children, who were treated with old tuberculin intradurally. In the first case treated, the child had general miliary tuberculosis; there was some betterment of nervous symptoms following the injection, but three days later the child died. In two other cases, in which the diagnosis was confirmed by the finding of tubercle bacilli in the spinal fluid, complete recovery followed within twenty days after three and two injections, respectively. In all the cases following the injection, instead of the expected rise, there was a fall of about 1° C. in temperature. The author suggests an initial dose of 1 mg. old tuberculin. As a vehicle for the tuberculin, he recommends cerebrospinal fluid. Details of the cases are not given. This is unfortunate since the results which the author claims for his treatment are so important that full records of his observations would seem to be desirable. (The briefness of the present report in spite of the favorable results reported would seem to make it advisable to proceed with extreme caution before repeating this work. The number of observations which the author reports is too small to have determined the safety of the treatment or the dosage of tuberculin, it would seem.)

A Case of Balantidiosis Treated with Emetin.—R. Axter-Hasenfeld (*München. med. Wchnschr.*, 1915, lxii, 152) reports a case of balantidiosis treated with emetin. For four months, the patient, a woman, aged sixty years, had suffered with a severe diarrhea. She had been given various remedies, she said, without result. There were as many as twelve watery stools daily, containing pus and blood. The patient was weak and emaciated. On physical examination, the internal ternal organs were normal, except the colon. The stools showed Balantidium coli, as many as ten in a field, actively motile. The author administered uzara at first with slight improvement. The patient, however, was still having about eight stools a day. Then he gave 0.03 gm. of emetin hypodermically. In the following twenty-four hours, the patient had only one stool. The same dose was repeated daily until eight doses had been given. The consistency of the stools became firmer, the pus disappeared. After the third injection, the balantidia could no longer be found. The patient was permanently relieved. As balantidiosis is rare in the author's practice, and as the result of emetin treatment was so brilliant, the case is reported in the hope that others may determine whether the drug is a specific in this infection.

The Extent of Protein Digestion in the Presence of Hydrochloric Acid Deficit.—At the suggestion of Prof. Krehl, L. Pel (*Deutsch. Arch. f. klin. Med.*, cxii, 369) has attempted to determine whether the hydrochloric acid deficit sometimes observed after test breakfasts or test meals necessarily means extended cleavage of protein. For the determination of free hydrochloric acid and hydrochloric acid deficit he has employed Günzburg's reagent as indicator. The total acidity has been estimated with litmus paper. The total chlorides were estimated by the method of Lüttke and Martius. An approximation of the extent of proteolysis has been arrived at by determining total nitrogen (Kjeldahl) and amino-nitrogen by the method of Van Slyke. All the values have been calculated on the basis of 100 c.c. gastric juice and also on the basis of 100 gram nitrogen. The acidity has been expressed in cubic centimeters of tenth normal NaOH, the nitrogen in cubic centimeters of tenth normal NH_3. The binding or uniting power (Bindungsvermogen) has been calculated; if free HCl is present this represents the difference between total HCl and free HCl, while with a deficit it is the sum of the deficit and the total HCl. The author has made numerous observations on the filtrates from test breakfasts and test meals. His general conclusions are as follows: (1) The amino-nitrogen, measured by Van Slyke's method, is generally higher relatively after a test dinner than after a test breakfast. (2) The amino-nitrogen, as compared with the total nitrogen, is increased in some cases with hydrochloric acid deficit, not in others. For example, the author found 9 per cent. amino-nitrogen with a deficit of 119 in one case, 14 per cent. amino-nitrogen with free HCl of 68 in another. (3) The HCl-binding power and the amino-nitrogen content, given a like quantity of total N, do not necessarily run parallel, though in some cases one does find high binding power and high amino-nitrogen combined. Extended cleavage of protein is, therefore, not the only reason for high HCl-binding power. Rather it must be supposed that the special nature of the undigested or slightly digested proteins is responsible in many cases. (4) The HCl-binding power is increased in some cases of deficit not in others. It is practically never sufficiently increased to account for the deficit alone. (5) Among the causative factors in the production of a deficit the most important is an acid secretion inadequate for the amount of nitrogenous bodies present. Differences in the degree of cleavage of the proteins is of secondary importance. Thus in two cases with practically the same HCl-binding power and the same degree of cleavage the free acid was 68 in the one with a deficit of 24 in the other. (6) Thus there are two kinds of deficit, the one with normal protein digestion the other with abnormally extensive hydrolysis of the portein. So far Pel has been able to discover no differential diagnostic value through determining which of these is present.

Nucleinic Acid in Blood Diseases.—W. Konnecke (*Deutsch. Arch. f. klin. Med.*, 1914, cxv, 177) has undertaken the study of experimental leukocytoses in primary blood diseases, as the results recorded in literature have to do almost entirely with the reaction obtained in normal individuals or those whose blood has been only secondarily affected. Of the various substances employed to produce a leukocytosis, Könnecke found sodium nucleinate given intramuscularly was the most suitable. It was found that the effects of the sodium nucleinate varied according to the functional ability of the bone marrow. Thus, a normal bone marrow whose cells mature more rapidly under the action of nuclein sends a larger number of ripe cells into the blood stream; the result is a moderate leukocytosis. The bone marrow in chlorosis and many secondary anemias (post-hemorrhagic, for example) is hypersensitive, the result being a more marked leukocytosis. In pernicious anemia and many forms of secondary anemia, on the other hand, the marrow was less sensitive than normal, or entirely insensitive to nuclein. In other words, the leukocytosis was slight or entirely lacking. In lymphatic leukemia only the myeloid system reacts. Severe cases of myeloid leukemia show no reaction to nuclein. In mild cases there is a decrease in the total white count following the first injection, due, Könnecke says, to lessening in the number of immature cells. After repeated injections, a leukocytosis may supervene, but if the injections are long continued, the organism becomes accustomed to the irritant and fails to react. The result of the reaction to sodium nucleinate permits one to draw certain conclusions as to the functional ability of the bone marrow, Könnecke says, which may be of value both in diagnosis and prognosis.

A Study of the Kidney Function in Congenital Cystic Kidney.—W. H. Veil (*Deutsch. Arch. f. klin. Med.*, 1914, cxv, 156) has had the unusual opportunity of studying carefully three cases of congenital cystic kidney diagnosed clinically. His attention was directed especially to the examination of the functional capacity of the kidneys. In all three cases there were bilateral, palpable, polycystic renal tumors. In all of the cases the results of the functional study was the same. Veil found a marked decrease in the ability of the kidney to secrete a concentrated urine, though the diluting power was retained. This inability to concentrate was shown by the passage of normal quantities of urine when the patient was on a diet poor in salt and nitrogen, with polyuria when the usual mixed diet was given. Otherwise there was no diminution in the ability of the kidneys to secrete nitrogen, sodium chloride and water, but for substances foreign to the body (milk-sugar, potassium iodide and phenolsulphonephthalein) there was a moderate delay in excretion. The finding of traces of albumin in the urine without morphological elements was constant. There was a moderate increase in blood-pressure amounting to 235 to 240 cm. water (v. Recklinghausen). The study of the blood in these cases revealed normal concentration, osmotic pressure, and rest nitrogen.

SURGERY

UNDER THE CHARGE OF

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Complete Fracture of the Lower Third of the Radius in Childhood, with Green-stick Fracture of the Ulna.—Skillern (*Annals Surgery*, 1915, lxi, 209) says that there is a fracture of the lower third of the radius and ulna peculiar to childhood, which constitutes about 13 per cent. of fracture of the forearm. This fracture commonly occurs before the age of puberty, is most frequently encountered during the summer months, and is caused usually by the effects of gravity plus momentum. It is characterized by complete fracture of the radius with dorsal and lateral displacement of the lower fragment and by incomplete green-stick fracture of the inner half of the ulna, usually, at a higher level, the outer half remaining intact and maintaining the deformity of the ulna, which is a bowing of the lower fragment toward the radial side and which in turn, maintains the displacement of the distal fragment of the radius. In reducing the displacement the aim must be to convert the incomplete green-stick into a complete fracture by forcibly rupturing the still intact outer fibers, thereby enabling restoration of alignment of the distal fragment of the ulna with that of the axis of the bone, the distal fragment of the radius coincidently shifting itself automatically into position. The criterion of reduction is the restoration of the normal alignment of the inner border of the ulna. Fracture of the lower third of both bones and of the radius alone comprise 70 per cent. of fractures of the forearm in childhood. The site of the fracture and its variety may often be predicted by a knowledge of the history and mechanism of the fall. Injuries to epiphyses, whether strain, sprain, or disjunction should be recognized and treated as fractures because of their importance in the growth of the bones and because epiphyseal injuries often predetermine infections, typically tuberculous. Diagnosis may be established clinically by the mechanism and "wincing" tenderness. If deformity exist it is unjustifiable to elicit further signs of fracture. Roentgenograms are of corroborative value, but by no means the final arbiters. Their chief value is in showing the degree of deformity and its presence after reduction. Owing to the delicacy of the radius and ulna in childhood fracture is the rule, while contusion and sprain are the exceptions. Treatment is begun by the administration of an anesthetic if deformity exist. Otherwise a carefully prepared and padded splint (or splints) is applied firmly and without undue pressure. Roentgen-ray control of reduction is important. Massage and passive motion are adapted to the individual case. The splints must be removed as soon as there is firm union. Operation is indicated only when conservative treatment is admittedly a failure. It will seldom be necessary. The inlay method of Albee should be used instead of an array of metal fixtures.

Ureteral Calculi; Special Means of Diagnosis and Newer Methods of Intravesical Treatment.—GERAGHTY and HINMAN (*Surg., Gynec. and Obst.*, 1915, xx, 515) base their observations on 67 cases from the urological clinic of the Johns Hopkins Hospital. They say that the symptoms of ureteral calculus are not diagnostic and are insufficient to definitely determine either its presence or position except in rare instances. While radiography is the simplest and probably the most valuable single diagnostic method for the detection of ureteral calculi, even in the most expert hands, a surprisingly large percentage (22.4 per cent.) may be undetected by it. This large percentage of failures demands the employment of supplementary methods before excluding stone with any degree of positiveness. By means of collargol ureterograms a calculus occasionally will be shown which the simple Roentgen-ray failed to reveal. The employment of the wax-tipped catheter is by far the most accurate method for the detection of ureteral calculi, and this method should be in more general use. In 6 out of 30 cases of ureteral calculi (20 per cent.) seen in the last two years, it has located a stone where repeated roentgenographs were uniformly negative. Owing to the great frequency of extra-ureteral shadows in the region of the pelvic portion of the ureter, diagnosis of ureteral stones in this region cannot be accepted without confirmatory information. A considerable number of stones which enter the ureter pass spontaneously, and the discovery of a small calculus is not always an indication for immediate operative interference. Unless the stone is blocking completely or producing repeated and violent colic, simple and manipulative methods should first be employed. For calculi beyond the juxtavesical portion, displacement with the ureteral catheter, injection of oil or the securing of relaxation of the ureteral wall by using the thermocatheter may, in certain cases, result in the expulsion of the stone. When the stone is in the vesical portion of the ureter, cystoscopic procedures should usually be successful. A study of these cases, as well as different series reported in the literature, shows that a considerable portion (14.3 per cent., Geraghty and Hinman; 17 per cent. of

204 cases, Jeanbrau) of ureteral calculi are arrested in the intramural portion of the ureter—a portion which can be readily reached by cystoscopic methods. These methods, therefore, have an increasing field of usefulness.

Periosteal Regeneration of Bone.—Smith (*Surg., Gynec. and Obst.*, 1915, xx, 547) says the following conclusions are drawn from considerable experimentation carried on at several different institutions, some under very adverse conditions and others under favorable circumstances. The results obtained were absolutely contradictory to each other. This clearly demonstrates that the cellular elements of the stripped periosteum are dependent upon a varying personal factor. It is possible at the present time to vary the end results according to certain technique; the periosteum stripped quickly and with a sharp periosteotome will produce bone in a greater percentage of cases if young animals are used than if fully developed adult animals are employed. Likewise a greater percentage of positive results will be obtained with periosteum which is stripped slowly and with an elevating action of the periosteotome than when the periosteum is quickly torn loose from the compact bone. A very large percentage of positive results can be obtained by using very young animals and small strips of periosteum. Fibrin is a very active stimulant to osteoblastic activity. In the clinical utilization of these facts, many important factors must be taken into consideration with respect to the end results desired; *i. e.*, stage of bone development; care with which the subperiosteal resection is performed; ample allowance should be made for satisfactory conditions suitable to fibrin formation and a generous supply of blood to the part provided for.

The Nervous System and Abdominal Affections.—Thies (*Mitt. a. d. Grenz. geb. d. Med. u. Chir.*, 1915, xxvii, 415) says that in diseases of the intestinal tract one often observes enlargement or diminution and usually a difference in the size of the pupils, or in the opening between the eyelids. The further oralwards the disease in the intestine, the less frequently is the difference in the pupils or eyelids found, and the further rectalwards the disease, the more frequently. These eye symptoms are found with especial frequency in diseases of the organs supplied by the sacral-autonomous nerves, as in the large bowel, the genital organs and the urinary bladder. The difference in the pupils is found more frequently than in the opening of the eyelids, especially in diseases of the upper intestinal tract. A difference in the pupils or opening of the eyelids is only rarely found in affections of the kidneys. It is likewise usually absent in affections of the gall bladder without participation of the large bowel. The difference in the pupils or opening of the eyelids disappears, as a rule, after the removal of the local abdominal focus of disease or it is diminished. Occasionally one finds later a reverse difference.

Management of the Convalescent Stage of Hip Disease.—Packard (*Amer. Jour. Orthop. Surg.*, 1915, xii, 666) says that he has seen many cases of hip disease in the past year, where the treatment had been discontinued while the patient was in the convalescent stage. These cases were free from pain, but the limbs were generally flexed and adducted, and in many instances the lameness was increasing, motion was present in some case but generally absent. From his experience he concludes that: Many cases of hip disease are discharged as cured while the disease is still in progress. Great care must be exercised in determining the joint condition, and protection should be continued as long as indications of the disease are present. Repeated Roentgen-ray pictures must be taken as an additional guide for treatment. The deformity of flexion and adduction should be prevented during treatment, but if present, corrected without trauma to the joint. If for any reason there is the slightest evidence of a relapse after the treatment has been discontinued, immediate protection of the joint is demanded. To obtain the best result one should not be content with methods which demand the least time, or nature's cure supplemented by osteotomy, but should always utilize the means that best meet the indications, regardless of the expenditure of the surgeon's time.

The Futility of Arterio-anastomosis in the Treatment of Impending Gangrene of the Lower Extremity.—STETTIN (*Surg., Gynec. and Obst.*, 1915, xx, 381) did a series of eighteen experiments, his aim being to find some way of graphically recording the amount of the arterial circulation possible through venous channels and he called upon the Roentgen rays as an aid. He used lower extremities, freshly amputated, in cases of gangrene from arteriosclerosis or other arterial disease and variously injected these with liquids impenetrable to the Roentgen rays. He says that the arterial circulation to the periphery, even in very advanced arterial disease, is in every respect better and easier than the retrograde venous circulation, mainly because of the obstruction offered by the valves and the short circuiting of the blood through anastomoses of neighboring venous collaterals. The operation is dangerous and the results have been most unsatisfactory, except in a small percentage of cases. The few so-called successful results have been obtained probably more in spite of than because of the operation, inasmuch as various factors play a role in the improvement in these cases, as improvement has been recorded after definite closure of the anastomosis, and as failure has occurred with perfect patency of the arteriovenous fistula. Even if the anastomosis functionates, which it rarely does, there is no possibility of circulatory improvement, but rather quite the reverse. The term "reversal of the circulation," at least so far as clinical cases are concerned, is absurd. Even if the usefulness of the operation were proved beyond question, the possible indications would be restricted to an unappreciable minimum. Stettin, therefore feels that the scepticism of Lejars, Lenormant, and Wettstein is a trifle too mild. Even Coenen is not quite emphatic enough. Stettin rather agrees with Guthrie, who, although having once claimed to have shown with Carrel the possibility of reversal of the circulation in the limb of a dog, deplores the fact that arteriovenous anastomosis should have been applied to the human being for circulatory disturbances of the lower extremity and prophesies its failure; for he, Stettin, believes that it is very questionable if the operation is ever justified. He believes that this procedure should be entirely eliminated from our surgical repertoire.

THERAPEUTICS

UNDER THE CHARGE OF

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The Effect of Lumbar Puncture in Delirium Tremens.—STEINEBACH (*Deutsch. med. Wchnschr.*, 1915, xli, 369) says that the cerebral pressure is increased absolutely in most cases of delirium tremens and probably is relatively increased in all. He found the cerebrospinal fluid under considerable pressure in one patient who showed inactive pupils to light—and the delirium subsided immediately after a lumbar puncture. He says that Schott-Müller has claimed that in acute alcoholic intoxication the cerebrospinal fluid is always under increased pressure and that alcohol is present in the fluid. Acting upon these observations Steinebach has systematically applied lumbar puncture for the treatment of delirium tremens. His results have confirmed his impression that the abnormally high pressure is responsible for the symptoms of delirium. He does not believe that the alcohol content of the spinal fluid is directly responsible for the delirium but is inclined to attribute the symptoms to a combination of high cerebral pressure, with a secondary poison generated by the alcoholic intoxication. The relief of symptoms following lumbar puncture is due not only to a regulation of the pressure but also to the renewal of a certain amount of poison accumulated in the cerebrospinal fluid under tension.

Kaolin and Blood Charcoal in the Treatment of Diarrhea Processes.—WOLFF and EISNER (*Therap. d. Gegenw.*, 1915, lvi, 92) says that bolus alba (Kaolin) which has been recommended for years as the best treatment for cholera has been proved most efficient by the experiences in the present war. It seems to act by absorbing the toxins and mechanically engulfing the bacteria and carrying them away with it. Blood charcoal acts very similarly and the two can be used in combination. He gives details of twenty-five cases of various diarrheal diseases including dysentery and typhoid fever, showing the almost immediate arrest of the diarrhea after the use of kaolin and charcoal. The kaolin and charcoal can be given in oatmeal gruel, care being taken to prevent them from settling to the bottom by constant stirring. This method of treatment was also used with apparent success in some healthy bacillus carriers, no bacilli being found in their stools after treatment. The author adds that no treatment is so simple nor is it easy to imagine anything more harmless.

The Treatment of Typhoid Fever with Dead Cultures of Typhoid Bacilli.—GOLDSHEIDER and AUST (*Deutsch. med. Wchnschr.*, 1915, xli, 361) report a series of fifty-seven typhoid patients treated with good results by vaccine made with killed cultures of typhoid bacilli. They found that, after a preliminary increase in the fever which at times lasted several days, the temperature frequently fell by crisis with corresponding improvement in the remaining symptoms. They warn against its use in the event of a complicating pneumonia, intestinal hemorrhage, a weakened cardiac action, or in cases in which the temperature is at an abnormally high level.

The Treatment of Typhoid with Autogenous Living Vaccine.—Bourke, Evans and Rowland (*Brit. Med. Jour.*, 1915, 2831, 584) after treating cases of typhoid fever with the ordinary vaccine and obtaining excellent results were led to try the effect of autogenous living vaccine as a therapeutic measure in typhoid fever. Their cases have demonstrated that this method of injecting living bacilli in suitable doses is perfectly safe. The vaccine was injected subcutaneously, as a rule in the pectoral region and was followed by a very slight local reaction, but a marked general reaction. The injection, as a rule, was followed by a sharp rise in temperature within the first few hours followed by a marked fall within twenty-four hours after the injection. Careful notes were made and in their minds there is no doubt that this treatment had a beneficial effect and tended to cut short the duration of the disease. It promotes perspiration, the aspect of the patient undoubtedly becomes brighter after injection, and the tongue becomes much cleaner. The disease was in each case diagnosed by means of blood culture. For this purpose 5 c.c. of blood were drawn from the arm and immediately transferred to 1 per cent. sodium taurocholate. From this a broth culture was prepared, and the purity and identity of the growth verified by agglutination and sugar fermentation tests. The broth culture was reinoculated into fresh broth every day and itself constituted the vaccine. No further preparation whatever was employed. The age of the culture used was generally eighteen hours, and the number of bacilli contained in it was obtained by a direct method of counting. The average number of organisms ranged from 60,000,000 to 300,000,000. They believe that their observations demonstrate that a living culture of the typhoid bacillus can be injected subcutaneously into enteric patients, not only without any deleterious effects, whatever, but, as far as the cases reported show, with decided favorable influence on the course of the disease.

The Destruction of Tetanus Germs with Ultra-violet Rays.—Jacobsthal and Tamm (*Münch. med. Woch.*, 1914, lxi, 2324) report that radiation of jagged wounds with ultra-violet rays will kill tetanus bacilli and the bacilli of malignant edema at the site of infection. They believe that systematic use of this method of treatment will help to prevent systemic infection. This method should not replace thorough surgical cleansing of the wound but should supplement the surgical treatment. Kromayer's lamp and the artificial high solar light may be used to generate the ultra-violet rays.

The Action of the Opium Alkaloids on the Coronary Artery and the Coronary Circulation.—Macht (*Jour. Am. Med. Assn.*, 1915, lxiv, 1489) says that morphin, the principal opium alkaloid, produces a mild relaxation or dilatation of the coronary artery and an increase in the coronary outflow; narcotin produces the same effect in a greater degree, and papaverin gives certainly the most marked vasodilating action of them all. On the other hand, the vasodilator effect of codein on the coronary is very slight, and that of narcein and thebain practically none at all. A most interesting phenomenon noted is the peculiar result of the synergism, or antagonism as it might better be called of morphin and narcotin. A combination of these two alkaloids instead of producing a vasodilatation, as might be expected produces practically no dilator effect at all. This antagonism apparently exists only in the dilator action of narcotin and morphin. In his experiments, Macht found that narcotin is by no means an inert drug but is quite toxic to the heart, respiration and other physiologic functions. The effect of combining morphin and narcotin seems to be rather a true synergism in which the two components play equally important parts. To a lesser extent a similar synergism has been noted between morphin and papaverin, and codein and narcotin. The commercial combinations of opium alkaloids of Straub and of Sahli were found to produce very little vasomotor change in the coronary circulation. It is hardly necessary to declare that these differences in the behavior of the different alkaloids may be of practical importance. Thus, for instance, in cases of coronary spasm, which is regarded as the commonest cause of angina pectoris, an opiate possessing a marked vasodilator action would certainly be preferable. J. Pal of Vienna, who has worked a great deal with papaverin, has actually recommended and employed that drug in angina pectoris and other conditions with vascular spasm. In choosing a suitable drug, other factors are, however, to be borne in mind. The principal other factors to be considered in the case of an opiate are its narcotic and analgesic action, its effect on the respiratory centre, and its effect on the heart. In respect to narcosis and analgesia of the six alkaloids studied, narcein and thebain fall out of consideration. These alkaloids, though derived from opium, have no sedative action. Indeed, thebain is a convulsant much like strychnin, and narcein has also an exciting rather than sedative influence on the central nervous system. Narcotin also has very little effect on pain. Of the three other alkaloids remaining, the narcotic and analgesic properties of morphin and codein are too well known to need reiteration. It is not generally known, however, that papaverin is quite an efficient drug in this respect, though attention was called to that effect by Baxt as early as 1869. In regard to action on the respiratory centre of the three drugs, morphin, codein, and papaverin, the morphin is certainly the most depressant. Macht states that papaverin is much less depressant than morphin in this respect, and codein still less so. As to the action on the heart, it may be also stated in this connection that narcotin has the most toxic action of the alkaloids studied; and morphin, though not very poisonous, is in full doses depressant to the heart. Codein and papaverin, on the other hand, were found to have no depressant action in this respect, and in small doses were found actually to stimulate cardiac activity. Inasmuch as all opium alkaloids in excessive quantities are depressant to the heart, and inasmuch as caffein is one of the chief pharmacologic antidotes to opium and is at the same time a cardiac stimulant, it was of interest to learn the action of a combination of caffein and some of the alkaloids studied. Accordingly, some experiments along these lines were made.

It was found that caffein alone dilates the coronary artery, and that this action is not antagonized by the opium alkaloids. Thus a combination of papaverin and caffein gave a dilatation of the coronary ring. In respect to the cardiac effect, it was found that caffein, given simultaneously with an opiate, produced cardiac stimulation and counteracted any cardiac depression that might otherwise have occurred Macht hopes that these observations may conduce to a more rationa therapy of cardiac conditions.

The Indications for the Subcutaneous Use of Magnesium Sulphate in Traumatic Tetanus.—Usener (*Münch. med. Woch.*, 1914, lxi, 2323) writes especially concerning the treatment of tetanus by subcutaneous injections of magnesium sulphate. He believes that it is of real value and should be used in large doses under conditions which directly threaten life—such as severe dyspnea due to tetanic spasm of the respiratory muscles, severe spasms of the esophagus, etc. The subcutaneous use of magnesium also lessens the number and severity of individual convulsions. The intradural use of magnesium should be reserved for the very urgent cases—as untoward effects, such as paralysis of respiration, are frequently seen. With regard to the strength of solution to be used for subcutaneous injection, Usener advises a solution of from 40 to 50 per cent. strength for adults in dosage of from 0.15 to 0.2 g. per kilo. In light cases a single dose may be sufficient but in severe cases and when it is necessary to secure the full effect of the drug, three or four doses at two-hour intervals should be given. In order to maintain the effect of the remedy its administration should be continued until the symptoms calling for its use have disappeared.

The Intravenous Injection of Mercurialized Serum in Syphilis.—Thompson (*Jour. Am. Med. Assn.*, 1915, lxiv, 1471) has devised a method of administering mercury intravenously without the unpleasant results (phlebitis and periphlebitis) which occasionally occur after the intravenous injection of mercurial salts in watery solution. He makes use of mercurialized serum and gives the details of its preparation in his article. In brief, the serum is prepared by adding an aqueous solution of mercuric chlorid to blood serum so that 7 c.c. of the mixture contains one-third grain of mercuric chlorid. Mercury albuminate which is at first precipitated on the addition of the serum is completely dissolved when an excess of serum is added; and is kept in solution indefinitely by heating the mixture in a water-bath for one-half hour at 55° C. The mercurialized serum can be kept indefinitely in sealed ampoules. Thompson gave 1.75 c.c. of the serum (equivalent to $\frac{1}{12}$ grain of mercury) as an initial dose and gradually increased this dose to 7 c.c., the equivalent of $\frac{1}{3}$ grain of mercuric chlorid. Symptoms of mercurialism developed after comparatively small amounts of mercury had been given in this way. He says in conclusion that the intravenous method of administrating mercury is not the method of choice in all cases of syphilis, but is so in certain cases, in which quick results must be brought about, and in those cases in which great pain occurs in intramuscular injections of mercury.

PEDIATRICS

UNDER THE CHARGE OF

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Ameba Colitis in a Child of Five Years.—G. J. GREIL (*Archiv. Pediatrics*, 1915, xxxii, 272) reports a case of ameba colitis in a child, aged five years. The condition began with distention and pain in the abdomen, and developed gradually into emaciation, with many blood-tinged movements a day, severe abdominal pain, and distention. On examining the stools, actively motile amebas were found. Marked improvement followed two hypodermic injections of one-tenth grain and one-eighth grain respectively during twenty-four hours. Emetin, grain one-sixth, was given every two days for three or four doses, and the child apparently recovered by rapid degrees after this. The stools were examined at the end of three weeks and again in one month, amebas were found, and the emetin given every other day for six doses. The examination at the end of this third month was negative and the patient declared cured. The case illustrates the importance of thorough and continued examination even when the patient is apparently well.

Early Pulmonary Tuberculosis in Childhood.—KENNETH FRASER (*British Jour. of Tuberculosis*, 1915, ix, 1) gives an analysis of the study of approximately 300 cases of pulmonary tuberculosis among children in elementary schools. Out of 29,750 children attending elementary schools in one county, 296 cases of pulmonary tuberculosis were diagnosed. The percentage distribution was: Whole county, 0.8 per cent. Rural: boys, 0.8 per cent.; girls, 0.7 per cent. Urban: boys, 0.8 per cent.; girls, 0.9 per cent. In point of age, the number of cases increases rapidly from 19 at five years to 37 at six years, 38 at seven years, and 40 at eight years. These figures seem to constitute a serious indictment of the influence of schoōl life on children predisposed to tuberculosis. The returns for weight and nutrition of these cases is striking. Of this series 24 per cent. were above average weight, 10 per cent. were of average weight, and 64 per cent. were below average weight. Nutrition must be considered with weight, and at least 40 per cent. of this series showed signs of impaired nutrition, which is probably the first visible sign of tuberculosis infection. Night sweating occurred in 55 per cent. of the cases. This has no weighty significance unless the sweats are markedly heavy. Coughing occurred in 45 per cent. of cases, the dry "hacking" cough being particularly significant of incipient phthisis. In this series, in only 1 case was neither apex involved, in 76 per cent. the apices of both lungs were affected. Where one apex alone was involved the right showed three times to once in the left. Moderate dulness occurred in 40 per cent., marked dulness in 91 per cent., and very slight dulness in 23 per cent. of the cases. Friction, denoting pleurisy, and fine crepitations when localized and persistent are the most valuable auscultatory signs. Within two years, 214 reëxaminations were made and indicated that spontaneous improvement is more common in girls than in boys, that it tends to increase from the sixth year onward, and that rural areas have a much greater tendency to develop spontaneous improvement than urban areas.

Prognosis and Treatment of Congenital Syphilis. A Plea for Notification.—LEONARD, FINDLAY, and MADGE ROBERTSON (*Glasgow Med. Jour.*, 1915, lxxxiii, 330) give a synopsis of results obtained with different methods during the last two years. The following methods were tested. Cases treated with mercurial inunction and in breast-fed children the administration of pot. iod. and hyd. perchlor. to the mother. This method uniformly shows a high death rate from the reports of other investigators and the authors' figures in 18 cases show a mortality of 66 per cent., and of 71 per cent. for children under three months. Cases treated with joha and neosalvarsan by intramuscular injections and mercurial inunction showed fairly good results but the method was discarded on account of the great pain, the necrosis, and sloughing which often occurred. Cases treated with neosalvarsan by intravenous injections and mercurial inunction; in all, 43 cases were so treated. In younger children the veins of the scalp and in older children the external jugular vein was used. Concentrated solutions were used, 0.05 to 0.3 gram to 3 or 5 c.c. normal saline. Twenty-two of the cases were under three months and including all cases that died within a year of the last injection showed a mortality rate of 45 per cent. Antenatal treatment in 7 cases is reported. This is the treatment of pregnant women by neosalvarsan intravenously and by mercurial inunction. The result was good, the children at birth and at subsequent examinations showing no clinical signs of syphilis and having negative Wassermann tests. In no case was the course of pregnancy interrupted. The uterine localization of the disease accounts for the absence of clinical manifestations in mothers of syphilitic children. Congenital syphilis, even when vigorously treated shortly after birth is difficult to cure and has a high mortality. Of all the methods antenatal treatment with salvarsan would seem to give the best results from the above series and from the reports of Sauvage with 93 per cent. of cures and Bourret and Fabre with 100 per cent. of cures. For its proper execution, however, notification in some form or other is advisable and even essential, and syphilis should be added to this list of notifiable diseases so that the great number of cases be reduced by the proper treatment.

OBSTETRICS

UNDER THE CHARGE OF

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Indications and Contra-indications for the Use of Pituitary Preparations in Obstetric Practice.—VOGT (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) contributes an interesting paper based upon his observations in Kehrer's clinic in Dresden. He has been accustomed to use this drug at the end of the period of dilatation and during the stage of expulsion, especially when delay occurred through inefficient uterine contractions; also in the case of primiparas much above the average age for child-bearing, in deficient development of the uterus, in constitutional conditions depressing the patient, and in premature rupture of the membranes with escape of amniotic liquid, pituitary extract had given good results. In moderately contracted pelves where disproportion is not great, the writer obtained good results by giving pituitary extract. In contracted pelvis, however, the field for the use of pituitary extract is a very limited one. When the patient has had pains for some time, which grow weak, the disproportion between mother and child being a very moderate one, pituitary extract may be given to increase the power of uterine contractions. Care must be taken that the pelvis is not highly contracted, or the child excessively large, but in moderate degrees of contraction the Mercurio-Walcher position will be found especially valuable. Three illustrated cases are reported in which the use of pituitary extract seemed valuable. In cases where fever develops during labor, the use of pituitary extract brought about spontaneous delivery and spared the patient the dangers of operative interference in these cases. The writer has also had good results in giving pituitary extract when he was using dilating bags to expedite labor. The dread of operative interference is so strong in some that it is difficult to obtain permission to perform operations. In breech presentation where every effort is made to secure spontaneous expulsion, pituitary extracts may also be of considerable value. Those operations whose function it is to increase the size of the pelvis, such as hebostiotomy and subcutaneous symphysiotomy, will give better results if the use of pituitary extract be combined with the operation. The writer has little of personal experience to give in the use of pituitary extract in placenta previa. After Cesarean section this substance is useful, especially in cases where compression of the uterus has been made by a broad bandage during the time of actual delivery. The drug is useful and, when the placenta has been retained, the dangerous procedure of removing it by the hand may sometimes be avoided by giving pituitary extract, when the uterus will expel its contents spontaneously. In estimating the contra-indications for the use of the substance, he was unable to find evidence that pituitary extract entered the blood of the child when given to the mother during labor. It was possible, however, to bring on pains in this manner, so vigorous as to subject the child to unusual pressure, with its unfortunate result. As regards the mother, the drug should not be used when the condition of the kidneys is bad, as it is sometimes injurious and increases blood-pressure in such cases. It is interesting to observe that in a case of albuminuria with severe nephritis, and with a blood-pressure of 180, pituitary extract was given just after the child had been delivered by embryotomy. The drug seemed to have very little effect. In cases of cardiac disease, where the heart muscle is inefficient in maintaining circulation pituitary extract is not contra-indicated, but often acts as a stimulant, as do camphor, digitalis, and caffein. The strongest contra-indication is found in symptoms of threatened uterine rupture. The presence of the contraction ring should act as a warning against the use of the drug. Injurious complications arising from relief by pituitary extract must be rarely observed, as very few have been reported. The dangers in the use of the drug are few in proportion as it is correctly and carefully employed. It has no cumulative influence, and can be used at intervals of one or two hours at all stages of labor. The unpleasant symptoms sometimes seen, slowing of the pulse, threatened collapse, paleness, syncope, dilated pupils, sweating, and general depression, are peculiar to the individual patient. Occasionally very violent uterine contractions occur which are attended with considerable pain. Spasmodic contraction of the internal portion of the cervix and tetanus of the uterus have also been observed. In using these preparations the heart sounds must be watched by auscultation, when it will be noted that the fetal heart beat is often slower than normal. Thus the fetal heart has beat as slowly as 40 to the minute in occasionally observed cases. So the discharge of meconium is also a sign of dangerous pressure. Should the fetal heart be much disturbed the drug must be stopped, and prompt delivery effected by some operation. The writer has investigated a number of cases where death occurred in the child shortly after labor, or during labor, but had never found a case where the drug could be justly considered the sole cause of the accident. In mentioning the different preparations which he employed, five are enumerated: one an American preparation, one English, one French, and two German. The latter had been used in 7600 labors.

Changes in the Maternal Decidua Producing Complications During Pregnancy.—Hinselmann (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) has studied microscopically the parietal decidua in pregnancy when abnormalities in the chorion were present. He finds that violent impaction by the fetus is responsible for some of these conditions which has produced changes in the cells of some of the parts. Unquestionably, the amniotic liquid and also bacteria, have some influence. Necrosis is present in the deep layers of cells, or where there are channels through the decidual nuclei, the influence of the amniotic liquid can be excluded; so also, can possibly that of bacteria. In some of these cases hydrorrhea develops, and in others areas in the chorion become necrotic, and complications on the side of the fetus may develop.

GYNECOLOGY

UNDER THE CHARGE OF

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Acute Traumatic Displacement of the Uterus.—The ability of a single, acute trauma to cause displacement of a previously normal uterus has often been called into question, and not a few gynecologists are inclined to doubt the possibility of such an occurrence. In a paper recently presented before the New York Academy of Medicine, however, Barringer (*Am. Jour. Obst.*, 1915, lxxi, 758) reports six cases in which she believes this type of displacement to have occurred. The ages of these patients ranged from fifteen to forty-three years; all but one were nulliparæ at the time of the accident. In two cases the accident consisted in a fall on the back or side in the supine position, incident to being hurled from a car; in two others there was a sudden fall in the sitting position on the ice or a hard floor; in one the history was of a sudden unexpected strain in lifting, while in the sixth case the exact nature of the accident could not be determined, as the patient lost consciousness at the time. All the women were confined to their homes for periods varying from a week to several months. The symptoms that have been most prominent in the author's experience in cases of this type may be divided into four groups, as follows: (1) Pain, usually in the lower portion of the back, over the sacrum and coccyx, sometimes in the region of the rectum, with painful defecation; (2) Bladder irritability, this being expressed by great urgency and frequency of micturition. It may be so severe as to dominate the clinical picture. (3) Change in type of menstruation. In one of the patients a uterine hemorrhage occurred immediately following the accident; in two, menstruation became painful, prolonged, and too frequent; one case had not menstruated since the accident up to time of examination, and one showed no change. (4) Characteristic posture and gait. The shoulders are generally stooped forward, with head carried slightly forward, the dorsal and lumbar spine held in a position of slight kyphosis, the whole appearance suggesting the posture of traumatic lumbago. The lower abdominal muscles may be more or more contracted, the patient supporting them with her hand; the gait is slow and guarded. On vaginal examination, the author usually found one of three conditions: either (1) the uterus had swung over 180° on its pivotal point in the pelvis. The fundus lying in third degree retroversion, with the cervix in its normal place; (2) there was a moderate degree of prolapse; or (3) the uterus was a whole had been driven back into the hollow of the sacrum in varying degress of retroversion, fundus and cervix being incarcerated there. Treatment of course consists in reduction as soon after the accident as possible. In one instance, in which the diagnosis was made a day or two after the accident the uterus snapped back into place; the young girl was kept on her abdomen for a week, and was warned to keep the bladder emptied frequently. She made a complete recovery, has since married, and has had no difficulty with retroversion of the pregnant uterus. In another case, in which a couple fo weeks had elapsed since the accident, congestion made the reduction more difficult, necessitating tamponing the posterior fornix, and the employment of hot douches. Recovery here, also, was complete and permanent, the patient having been followed for over five years. In a third cases the condition was discovered only after two months of great discomfort; here treatment by means of a pessary was necessary for weeks, and the uterus never returned to as perfect position as the others. The author emphasizes the importance of early diagnosis in these cases, since if the conditions remains unrecognized, the patient will probably drift into years of invalidism, from which she might have been saved.

Treatment of Chronic Ulcer of the Vulva by Salvarsan.—Fisichella (*Policlinico*, 1915, xxii, 485) says that he has observed in the past five years twenty cases of chronic, indolent ulcers of the vulva, in all of which the Wassermann was positive. He has come to consider syphilitic infection of great importance in the etiology of this local condition although in the one case in which he attempted to demonstrate spirochetes in smears from the ulcer, he was unsuccessful, probably owing to the fact that the patient had been subjected to vigorous local and systemic treatment. Clinicians, he says, have generally refused to consider vulvar lesions of this type syphilitic in origin, even when occurring in obviously syphilitic subjects, owing to the failure of the ordinary specific treatment with mercury and the iodides to effect a cure. Fisichella considers, however, that these lesions are in fact comparable to many others—such as some gummas occurring in bones and on mucous surfaces, certain cutaneous keratoses, etc.—which, while extremely rebellious to mercury and iodides, yield quickly to small doses of salvarsan. In support of this idea, he cites the cases of three prostitutes who came into his ward for treatment. In all of these women the Wassermann reaction was positive, and plain clinical evidences of syphilis were present. In addition to other lesions, all had indolent, phagodenic ulcers of the vulva of long standing. Active treatment by means of mercurial inunctions, biniodide, and KI, together with local antiseptic applications, had been without effect, but the changes produced after small doses of neosalvarsan were little less than marvelous. The drug was given by the usual intravenous method, starting with 0.15 gm., a second dose of 0.30 gm. being given four days after the first, and a third of 0.40 gm. five days after the second. Immediately after the first administration, improvement began to be noticed; healthy granulations were formed, and gradually cicatrization began from the edges, complete healing taking place in all three cases within fifteen days, notwithstanding the fact that these ulcers had resisted all other methods of treatment for years. Subsequent examinations of the patients have shown the result to be permanent, nothing remaining at the site of the original ulcer but a smooth, firm cicatrix, with a slightly pigmented border.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Elliott's Operation in Glaucoma.—Lundsgaard (*Klin. Monatsbl. f. Augenhk.*, February and March, 1915, p. 209) concludes from his experience with this operation that the procedure is a very valuable addition to the therapy of glaucoma, in suitable cases relatively certain in its results, and of facile execution. Three years additional experience with it, however, has convinced the author that this operation entails greater risk than he was first inclined to believe. He, therefore, does not now favor operating in every case of increased tension and would not, like Elliott, operate as a prophylactic measure. Where the tension is relatively low, 30 to 35 mm. without loss of field, miotics have given satisfactory results; where the tension is higher than 30 mm., especially if miotics are without effect, the writer operates in all cases of simple glaucoma, even where the fields have been markedly affected and the visual acuity lowered.

In secondary glaucoma (uveitis with increased tension) the reporter would be very conservative as regards operating. To avoid secondary perforation and infection he recommends making the conjunctival flap as thick as possible and he considers the iridectomy to be, to a certain extent, a preventive measure, in that it prevents secondary prolapse of iris, which event he believes favors perforation, for which reason the prolapse is to be excised whenever it occurs.

The Effects of Various Kinds of Rays upon the Crystalline Lens.—CHALUPECKY (*Wien. med. Wchnschr.*, 1914, pp. 27, 270) has attempted by suitable experiments to gain an insight into the mechanism of the occurrence of opacities of the crystalline lens, following the action of powerful sources of electricity as well as the influences of various kinds of rays. By means of chemical analyses and experiments upon guinea-pigs, he was enabled to confirm Widmark's views as to the direct influence of the ultra-violet rays upon the lens. On the other hand, he was unable to show by his experiments with the Roentgen rays, even with intense radiation, any chemical changes in the structure of the crystalline. A like negative result occurred in his experiments with radium chloride, with Roentgen rays and with mesothorium.

Glaucoma and Blood-pressure.—MACRAE (*Ophthalmoscope,* April, 1915, p. 168) examined 20 cases of primary glaucoma and a number of control cases with a view to determining the influence of the blood-pressure in glaucoma. His results are not uniformly either in favor of, or against, the theory that the average blood-pressure in glaucoma is high, though they tend to oppose that view. That the blood-pressure helps to maintain the eye tension, no one will deny, but the latter may be affected in many ways which have no connection with, and no effect on, blood-pressure; and conversely the blood-pressure may alter greatly without any corresponding observable effect upon the intra-ocular tension. That blood-pressure is of any importance at all in the causation of glaucoma is very doubtful. (It may be recalled that Dunn and Jackson have invariably found the blood-pressure above normal in primary glaucoma.)

Glaucoma in the Young.—From an exhaustive study of the clinical material of the University Eye Clinic of Tubingen, HAAG (*Klin. Monatsbl. f. Augenhk.*, February and March, 1915, p. 133) comes to the following conclusions: General diseased conditions, particularly disturbances of nutrition, were relatively frequent in this series of cases of juvenile glaucoma. Inflammatory glaucoma was about twice as frequent as simple glaucoma, with no decided difference in this respect between the sexes. Of the different states of refraction, myopia was relatively frequent, hypermetropia relatively rare; accordingly disposition of hypermetropic refraction to glaucomatous disease does not exist, while the former is true in the case of myopia; myopia is more frequent in simple than in inflammatory glaucoma. A deep anterior chamber is decidedly more frequent in inflammatory than in simple glaucoma; in fact it is only eyes with myopic refraction which present a deep anterior chamber. Heredity does not appear to play a greater part in juvenile glaucoma than in the same disease in older subjects. Congenital anomalies are frequently present in juvenile glaucoma. The writer's material presented no grounds for assuming an essential difference between the glaucoma of youth and that of age.

Impaired Vision Following Naked-eye Observation of Solar Eclipse.—SCHULER (*Heidelberg Dissert. Centralbl. f. p. Augen.*, April, 1915, p. 95) reports 26 cases of impairment of sight following the solar eclipse of April 17, 1912, treated at the Heidelberg eye clinic. The treatment there employed consisted of subconjunctival injections of sodium chloride, and the wearing of smoked glasses. More important than such therapeutic measures, the results of which must be doubtful in severe cases, would seem to be an effective prophylaxis. Much suffering might have been averted if, before the eclipse, the public had been enlightened as to the proper measures to be taken for the enjoyment of this rare spectacle. The public press should call attention to the danger of regarding the sun without well-darkened glasses, and even then for a few seconds only, etc.

Operative Treatment of Retinal Detachment.—ELSCHNIG (*Archives of Ophthalmology*, March, 1915, p. 163) summarizes his observations upon the treatment of retinal detachment as follows: Operative treatment is indicated in all cases that do not yield to conservative treatment within six weeks (How many do?). This time limit might be extended in those cases where an iritic irritation appears soon after the occurrence of the detachment. Cases of detachment following old iritis are not included. The operative procedures that come under consideration are: Scleral puncture with injection into the vitreous; and the Müller scleral excision. The less severe procedure should be practiced first, and if unsuccessful, should be repeated after a reasonable interval of time. If still unsuccessful, scleral excision should be carried out; only in cases with large retinal tears should this operation be practiced as a primary procedure. Operative interference should not follow too closely; six weeks at least should intervene. But indications and prognosis can only be established when the causes of the detachment are certainly known.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF
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The Incidence and Inheritability of Spontaneous Cancer in Mice.—Maud Slye (*Jour. Med. Research*, 1915, xxxii, 168) states that the phrase "inheritability of cancer" is used, although cancer as such is not inherited. The tendency to produce neoplasms, under the right stimulus, is as surely transmitted from generation to generation as is albinism, both in accord with Mendel law. Non-cancer-bearing strains can be had without the appearance of cancer; cancer-bearing strains can be had with the constant production of cancerous individual. Heterozyqous mice may be potentially cancerous, but do not produce cancer unless two heterozyqotes are mated. These results all obtained in the author's researches, and are fully demonstrated by carefully prepared charts. In-breeding as such has nothing to do with the transmission of cancer. The potentiality of the germ plasm to produce an individual whose tissues will proliferate into a neoplasm, under a given stimulus, seems to be the thing transmitted. The stimulus seems to be over-irritation at the point where the cancer arises. Cancer structures in mice are the same as those in man, they behave in the same way, and occur at points in close parallel to those in man. Tumors of the mouth and jaw are rare in mice; so, also, are chronic disorders of the oral region. Tumors of the stomach are common in man, but rare in mice. Inflammatory conditions of the stomach are rare in mice; and the intestinal disorders are acute only, followed in a few days by death of the animal. There is no case of tumor of the uterus or prostate gland, but there are no chronic disorders of these organs except hydrometria which usually does not persist. The first manifestations of the introduction of a cancer strain seem to be sarcomatous; later carcinomatous, the latter attacking the more differentiated tissues as the strain develops, and finally producing a preponderance of multiple tumors. In-breeding of cancerous strain tends to kill off the strains; out breeding tends to scatter the strain. The cancerous mice are among the largest, strongest, and most vigorously reproductive members of the strain, and only rarely does a weak mouse develop cancer. A decrease of food lowers the death age, lowers the rate of reproduction, increase deaths from ordinary infection, and does lower the cancer rate in that family. The author concludes: 1. An individual with poor normal growth has slow tumor growth. 2. An individual whose growth processes are used in reproduction shows slow tumor growth. 3. An individual of good growth power whose normal growth processes are not being used shows rapid growth of neoplasms. Infections take the weak; cancer takes the strong mice. Reduction of food increases infectability, lowers the cancer rate. Vigorous growth increases the cancer rate, lowers infection rate. Slight infection kills a frequent female, but tumor growth is slackened by frequency. Cancers occur only in cancer strain; infections occur in any strain. Infections spread in one or to other cages; cancer does not spread in the same cage nor to other cages by contact. Mice feeding on dead infected mice may become infected, but mice do not contract cancer by feeding on dead cancerous mice. Control mice fed on cancer material do not contract cancer. Cancer is a disease of middle and advanced age when normal growth processes are confined to regeneration and reproduction; infections are diseases of early life when growth processes are largely accretions in quantity and in complexity. Cancer differs from infection, since it follows the laws of heredity, and since it can be bred into or out of strain at will. Since cancer is transmitted, rather as a tendency to occur from a given provocation, an over-irritation, the elimination of over-irritation in one of cancer ancestry should materially lower the rate, and the eugenic control of mating so that cancer shall not be potential in both should also very materially decrease the incidence of human cancer.

The Prevention of Typhus Fever.—ANDERSON (*Public Health Reports*, April 30, 1915, p. 1303) discusses the recent work on typhus fever and the methods of its prevention and control based on these researches. He states that there is no experimental evidence to support the view that typhus is acquired in any manner other than by the intermediary of lice which have previously fed on persons sick with typhus. From this fact it is possible to deduce the fundamental procedures on which the control of the disease may be based, and these procedures may be grouped under four general headings: The first is, measures for the reduction of lice infestation among the population in general. These measures are, to a large extent, educational except in institutions and places over which the sanitary authorities have supervision, such as bath-houses, lodging-houses, and similar places. In surroundings where lice may find lodgment efforts should be made for the destruction of lice and their eggs. These efforts consist in the use of insecticides, both chemical and physical, bearing in mind the important point that the louse requires frequent feedings on blood and is, therefore, most apt to be found on recently used clothing or bedding. Under the second heading should be considered measures for the eradication of all lice and their eggs found on the bodies, clothing, bedding and surroundings of cases of typhus, suspects, and contracts. The first essential under these procedures is the institution of measures requiring the prompt reporting to the sanitary authorities of all cases of suspected cases of typhus fever. These cases should be promptly seen and the inspector satisfied that the surroundings are free from lice, in which case the patient may, without danger to the community, be treated at home. If, however, such is not the case, the patient should at once be removed to the hospital and the place from which he is removed should be treated for destruction of all lice and their eggs. All patients, suspects, and contacts should be bathed, the lice and their eggs in the hair and clothing destroyed, after which they should be given a clean change of clothing. They should then be kept under observation for twelve days. Under the third heading are measures such as should prevent or minimize the possibility of persons near cases of typhus being bitten by lice. It should be kept in mind that the radius of action of the louse is much shorter than that of the mosquito in yellow fever or the flea in plague. The transference of lice, and consequent infection with typhus, from one individual to another requires rather intimate association with lice-infested persons or their surroundings. And by reason of the fact that the louse requires frequent feedings to maintain life, this means for practical purpose surroundings recently occupied by persons and possibly by animals. Under the fourth heading it is suggested that persons desiring to enter localities in which the virulent form of typhus is prevailing in an epidemic form should be inoculated with the mild form of typhus fever so widespread in the United States, the case mortality of which is not over 1 per 100 while the case mortality of the typhus in Serbia, for example, is possibly 20 or more.

Diphtheria Bacillus Carriers.—ZINGHER and SOLETSKY (*Proc. New York Path. Soc.*, N. S., 1915, vol. xi) found that 4 to 8 per cent. of individuals in localities where diphtheria is endemic are carriers of bacilli morphologically and culturally like the diphtheria bacillus, but non-virulent in 30 to 50 per cent. of the cases. At the Willard Parker Hospital, Wilcox and Taylor found 4.5 per cent. of the cases admitted to the scarlet fever wards were bacillus carriers and of the isolated organisms only one-half were virulent. According to Neisser individuals who become persistent carriers after an attack of diphtheria show only non-virulent forms in fully 20 per cent. of cases. Such individuals could be discharged from quarantine if this fact were established. Roux and Yersin are of the opinion that both virulent and non-virulent are present in cases of diphtheria. The preponderance of each strain, however, varies with the severity of tbe disease, but that during convalescence all virulent strains undergo a definite diminution in virulence. Graham-Smith, Loeffler, as well as Park and Williams believe that the individual virulence or non-virulence is permanent with the strain. Dr. Williams and others have not been able to change the non-virulent into a virulent strain, as claimed by Thiele and Embleton for the Bacillus Hoffmani. It is probable that the virulent strains remain true to type and that the same applies to the non-virulent strains.

Non-virulent strains cannot be separated from the virulent by morphological or cultural characters. Hence, animal tests must be employed for this determination. M. Neisser uses a method analogous to that of Römer for the determination of small amounts of diphtheria antitoxin in sera. This consists of intracutaneous injection of varying mixtures of the unknown antitoxic serum and a standard antitoxin. A slight excess of toxin produces a local necrosing lesion, while a neutral or over-neutralized mixture shows no effect on the tissues at the site of injection. Zingher and Soletsky have improved Neisser's method by using 2 guinea pigs for the testing of from 4 to 6 different strains. One guinea pig serves as a control and receives about 200 units of antitoxin intracardially at the time of making the test, or intraperitoneally twenty-four hours before. Both pigs are injected with suspensions of the cultures to be tested intracutaneously. A fresh twenty-four-hour growth from an ordinary Loeffler slant is suspended in 25 to 30 c.c. of normal salt solution; 0.1 c.c. is injected into the skin. The results of the tests are noted in twenty-four to forty-eight hours. Virulent strains produce a definite local inflammatory lesion, which shows a superficial necrosis in forty-eight to seventy-two hours. In the control pig, the skin remains normal. With non-virulent strains no lesions will be found in either control or test animal.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Arterial Degeneration.—F. W. Andrewes (*Annual Report of Local Government Board*, 1913–14, Appendix B, p. 151) has been appointed to carry on a series of investigations on the nature and cause of arterial degenerations. The present is the second of his reports and is divided into two parts. The first line of investigation concerned the degree to which infectious conditions played a part in the premature occurrence of arterial disease. The second part of the investigation was to find some criterion by which the degree of degeneration could approximately be judged. Some very interesting findings are reported concerning the infective process of the arterial wall. The author not only studied the histopathology of the arteries but a bacteriological analysis was undertaken of the tissues of the larger arteries. By his technique he was able to obtain cultures of the arterial tissues quite apart from the presence of bacteria within the lumen. Out of six cases of Streptococcus septicemia the organism was isolated four times from the aortic wall, the staphylococcus was obtained twice out of three cases of septicemia, while in seven cases of malignant endocarditis the organism was not found in the arterial tissues. Similar negative findings were obtained in pneumonia. On the other hand, a positive result was once obtained out of five cases of acute rheumatic fever. Associated with B. coli infection the aorta was invaded by this organism in four out of five cases. These findings are important in the light of recent work demonstrating the presence of an inflammatory reaction in the arterial wall in many cases of infectious disease. Andrewes found that inflammatory reactions were present in Staphylococcus and Streptococcus septicemia, malignant endocarditis, scarlet fever, acute rheumatic fever, measles, B. coli infection, and syphilis. He points out that insofar as the destructive nature of the disease is concerned, syphilis stands by itself. The study, in general, confirms and amplifies those previously made by others. As every individual suffers not a few infective processes during his lifetime, each of which probably has some effect upon the vessel wall, the author believes it very suggestive that we here are dealing with the cause of premature arterial degeneration. In the subsequent investigation of finding an index of the grade of degeneration it was shown that the calcium content of the arteries is a useful criterion. The method, however, is too cumbersome to serve any other than a suggestive study. He found that the calcium content remained low and fairly uniform up to the twentieth year. From this until the thirty-fifth year there was a gradual increase, while after middle life, the calcium content rises markedly. Furthermore, it was found that the calcium contant of the arteries in disease was greatly increased and he believed that the relative amount is a good index of the degree of degeneration. For syphilis, however, these figures have not the same value, as the calcium content is not equally increased when syphilis alone is present, but varies with the association of it with a true sclerosis of the artery.

Cancer of the Thyroid in Graves' Disease.—Although we associate Graves' disease with certain structural changes of thyroid gland, not a few cases are on record in which the characteristic hyperplasia was wanting and an entirely different process present in the gland. Langhans classified the epithelial changes of the thyroid in seven groups, each of which has been described associated with Graves' disease. LYON (*Ztschr. f. Krebsforsch.*, 1914, xiv, 501) described a case of columnar cell cancer of the thyroid in a female, aged twenty-one years. She had typical symptoms of Graves' disease with enlargement of the right lobe. The tumor was removed as well as a number of cervical lymph glands which were involved in metastatic growth. The primary tumor as well as the secondaries contained more or less colloid. The growth was typically cancerous and infiltrated the gland capsule and surrounding tissues. The cancerous alveoli showed no papillomatous ingrowths as is usually seen in hyperplasia of the thyroid. The author believes that the new growth developed upon a primary hyperplastic goitre or that cancer and Graves' disease simultaneously developed in a colloid struma. Whether the colloid material produced in cancer of the thyroid is abnormal and assists in producing symptoms he was unable to say.

Tumors in Amphibia.—Recent studies on tumors have shown that they are widely distributed in all types of animals and particularly in vertebrates. Spontaneous tumors of rats, mice, fowl and fish are now well known to us. A number of investigators have described tumors in amphibia. The majority of these were located in the skin and were of the nature of fibroma, adenoma, and cancer. The first of these were described by Eberth, 1868, consisting of multiple adenomata of the skin of a frog. The character of the tumor in these animals is not easy to determine and some discussion respecting the origin of the tumor cells has arisen. It is suggested that the masses are associated with the presence of distoma and neomatodes which are so commonly present in the skin glands. Hypernephroma and tumors of the ovary have also been described. PENTIMALLI (*Ztschr. f. Krebsforsch.*, 1914, xiv, 623) observed multiple tumors beneath the skin of a frog which he was unable to transplant to new animals. Some of these tumors had ulcerated through the skin but not all were adherent to it. The small tumor masses were situated in the superficial portion of the corium. He believed that each of the multiple tumors was primary and not of metastatic origin. The tumor was of adenomatous type with some character of malignancy. They apparently began in the glands of the skin.

A Cytological Study of the Exudate in a Case of Tuberculous Pleurisy.—KIPP (*Folia Hematologica*, 1914, xviii, 43) studied the cells of a tuberculous exudate at intervals and observed the change in the relative counts from the acute process to the stage of healing. At the beginning an endothelial type of cell was found in greatest abundance. These, however, were not all of the same kind, some being true endothelial cells, others myeloblasts and some lymphoblasts. Subsequently the cell count changed and the proportion of lymphocytes increased considerably. Finally, at the end of three weeks the endothelial type of cell had almost disappeared while the eosinophiles and lymphocytes were the most prominent type present. The change in the cell count followed the clinical course from an acute to a chronic stage of the disease. He believes that the cytological study offers a means for prognosis. He furthermore points out that the cell picture of the tuberculous exudate is not a constant one and that a high lymphocytic count is not always present. The previous findings of others are extensively discussed in the text. The exact meaning of the increase of eosinophiles in tuberculous exudates is not well understood and is difficult of comparison in acute infections where their presence is so frequent in the late chronic stages. On the other hand, however, eosinophiles appear during the acute stages of some cases of sepsis, lues, cysticercus, influenza, and typhus. It is suggested that the eosinophiles in late tuberculous lesions appear as a local response and are associated with the myelocytes and certain forms of endothelial cells.

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ORIGINAL ARTICLES

A CONTRIBUTION TO THE PARALYTIC AND OTHER PERSISTENT SEQUELÆ OF MIGRAINE.*

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I. Introduction.
II. Migraine and ophthalmoplegia.
III. Migraine and permanent hemianopsia.
IV. Migraine and hemiplegia.
V. Migraine and optic nerve lesions.
VI. Concluding remarks.

I. Introduction. In the vast majority of cases, a tendency to migraine entails no more serious consequences than the recurrence of periodical headaches of varying degrees of severity. Headaches of this character are often associated with curious transitory focal symptoms, *e. g.*, scotoma, hemianopsia, hemiparesis, and hemiparesthesia. More rarely evanescent aphasic attacks and mental disturbances accompany the seizure. These focal manifestations are purely functional in nature and disappear promptly with the subsidence of the other symptoms of the paroxysm. They are generally regarded as manifestations of vascular spasm, and this theory is in harmony with their temporary and evanescent nature.

Attacks of this character may recur over a period of many years and yet leave no permanent mark or symptom. Unfortunately, this is not always true, and in rare cases permanent and often serious consequences ensue.

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* Read at a meeting of the American Neurological Association in New York, May 6, 1915.

The paralytic and other permanent complications of migraine may appear in various forms, viz., as ocular palsies (*migraine opthalmoplegique*), organic hemiplegia with aphasia, hemianopsia, and optic atrophy. A recurrent facial paralysis has also been ascribed to migraine (*facioplegic-migraine*), presumably of the same nature and having the same pathogenesis as the opthalmoplegic type of this affection.

The object of this study is to record my personal experience with a comparatively rare group of cases, and to emphasize the clinical fact that migraine, which is usually so harmless, may on occasion be the cause of serious and permanent sequelæ.

II. MIGRAINE AND OPHTHALMOPLEGIA.

CASE I. *Summary. Migraine in a woman, aged twenty-five years; following typical unilateral headache, developed complete paralysis of the left third nerve; recovery. One year later another migrainous seizure, followed by incomplete palsy of the right third nerve; recovery.*

History. Mrs. B., aged twenty-five years, married; has a child two years old; no miscarriages. No history of lues. Since birth of child has been subject to periodical headaches, which are always unilateral in character, and usually precede but sometimes follow the menstrual period. The pain is most severe in the temporal region, extending into the eye. The attacks are accompanied by nausea and often vomiting. There are no scotomata, or paresthesiæ, during the seizure. In severe attacks the pain lasts from two to three days. Her mother and one sister are subject to periodical headaches. An uncle on the father's side was epileptic.

The Attack. From August 8 to August 10, 1901, she had a severe unilateral headache of the usual migrainous type. On August 11, double vision and a drooping of the left eyelid appeared. The following morning there was complete ptosis on the left side. The pain was very great and centred chiefly in the left temporal region and eye.

Examination (August 16, 1901). Patient still suffers from severe pain in the left temple and eye. There is complete ptosis, with paralysis of the superior, inferior, and internal recti muscles on the left side. There is good movement of the external rectus and superior oblique. The pupils are equal and react promptly. No paralysis of accommodation. Ocular excursions of the right eye are normal. Other cranial nerves are negative. Optic disks are normal. General sensibility is normal, and there is no weakness of the extremities and no hemianopsia. The tendon and skin reflexes are present, and of equal intensity on the two sides; no Babinski. Heart action is normal. Urine is free from albumin and sugar.

August 28. Still has neuralgic pain in the left temple, forehead, and eye. There is considerable improvement in the ptosis and in the muscular movements supplied by the left third nerve.

January 3, 1902. Patient is still subject to periodical headaches at the time of the menstrual period. There is no trace of the former ocular motor palsy. She states that on December 25 she noticed some transient drooping of the left eyelid during a migraine paroxysm, but without diplopia.

Second Attack (November 4, 1902). The patient returns with the statement that she has had much less headache during the past few months, which is attributed to a gynecological procedure (dilatation of the cervix and curettage).

A few days ago, following a severe migrainous attack with the usual pain, on this occasion localized in the right temple, there appeared diplopia, but without ptosis. Dr. Alexander Duane, who made the ophthalmological examination, reports paresis of the right inferior rectus and inferior oblique muscles. Pupils are equal and react normally. The optic disks are normal. The paresis and accompanying diplopia disappeared during the course of the next few weeks.

COMMENT. This case may be regarded as a fairly typical example of the ophthalmoplegic migraine. A woman with hereditary hemicrania, develops during the paroxysm an oculomotor palsy. As is so common in the clinical history of this group of cases the pain was of the circumscribed variety, and localized chiefly in the temple and eye of the affected side. It was intense and very persistent. Of special interest is the alternation of the paralytic manifestations, appearing first on the left and then upon the right side. The recovery after both attacks was complete.

CASE II.—*Typical migraine since childhood; at the age of forty-three years had an attack of complete third nerve paralysis, with recovery; a subsequent attack which proved fatal; cardiovascular complications.*

History. A woman aged forty-three years; single; since childhood she has been subject to recurrent attacks of migraine. (A sister also suffers from migraine.) The headaches are always unilateral and usually upon the left side. When severe there is the usual termination in nausea and vomiting. In recent years the attacks have diminished in severity. As a rule the seizure is ushered in by scotoma (lights and colors). Between the paroxysms she is entirely free from cerebral symptoms. The menses still persist and are irregular. She states that for the last three years after very severe attacks there has usually been some *drooping of the left eyelid*, which would pass off in the course of a few days. There was never diplopia. During the past three months she has been subjected to a severe nervous strain, due to the serious illness of a parent.

The Attack. On June 23, 1909, she was seized with one of her usual headaches, which was preceded by the visual aura. The pain was situated in the left side, and was very severe. Late in the night it culminated in an attack of nausea and vomiting, after which she fell asleep. On awaking the next morning there was complete ptosis of the left eyelid, and on raising the lid she saw double. There was also a unilateral "drawing" sensation over the left side of the brow.

Examination (July 27, 1909). There is complete third nerve paralysis on the left side, with ptosis and dilatation of the pupil. All other motor cranial nerves are normal. There is slight hyperesthesia over the left brow, strictly limited to the supraorbital distribution of the fifth nerve. The left supraorbital reflex (McCarthy reflex) is absent. The optic nerves are normal. The right pupil is of normal size and reacts promptly to light and accommodation. The left pupil is widely dilated and stiff. The various tendon and skin reflexes are present and normal. No Babinski. Sensation and motion of the extremities are normal. Heart: There is a systolic bruit over the aortic cartilage and an accentuation of the second aortic sound. Systolic blood-pressure registers 200 millimeters. The urine contains a few hyaline casts and a trace of albumin. The Wassermann test is negative.

Subsequent History. The family physician reported that the third nerve paralysis cleared up completely in the course of three months.

A few months after her recovery, following a severe headache, there developed bilateral ocular palsies which terminated fatally; unfortunately, no more detailed information could be obtained of the symptomatology during this last attack.

COMMENT. This patient presents a classical history of migraine extending over a period of many years. In her forty-third year, after a typical paroxysm, a total left-third nerve palsy supervened from which she eventually recovered. In the subsequent attack, which was bilateral and progressive, she died. Even previous to the first attack she had noted after severe headaches a slight drooping of the left eyelid, which would pass off in the course of a few days. In the light of later events this may be regarded as an important warning signal of the paralysis which subsequently ensued. The great importance of cardiovascular changes as an etiological factor in this case cannot be questioned, and the occurrence of high blood-pressure and vascular degenerations in migraine should be regarded as complications with very serious possibilities.

It is interesting to recall in this connection the belief of some authorities, that prolonged and recurring attacks of vasomotor explosions such as take place in migraine over a period of many years are in themselves an adequate cause for the production of cerebral arteriosclerosis.

CASE III.—*Summary: The occurrence in two sisters with migraine of isolated abducens palsy developing during the attack; recovery.*

History. The patient is forty-seven years of age and a trained nurse. She has suffered from migraine since childhood. The attacks are peculiar in that the pain is always strictly localized, usually in the temple and brow of the left side. Very rarely the pain has appeared upon the right side, in which event it was always strictly limited to the region of the temple and brow. As a rule the paroxysms begin in the morning, lasting several hours and sometimes an entire day, but scarcely ever longer. After a night's rest she awakens free from pain. Toward the end of the paroxysm there is the usual nausea and often vomiting. The vision is a little blurred during the attack, but there is no scintillating or color scotoma, and no hemianopsia. These headaches are usually associated with the menstrual period, and since childhood intermissions longer than two or three months have been very rare. There is a strong family tendency to migraine, and her mother and four sisters have all been sufferers from this malady.

At the age of thirty she developed symptoms of exophthalmic goitre, which was treated surgically eight years ago by partial thyroidectomy; since which time she has been practically free from the symptoms of this disease. The menses were regular and normal up to a few months ago, when symptoms of the menopause made their appearance. She has been under severe nervous strain during the past year, caused by illness and death in her family.

The Attack. On January 26, 1912, she was seized with one of her usual headaches, the pain being situated in the right temple. The attack, however, instead of lessening after a few hours, as was usual, increased steadily in intensity and persisted, requiring frequent doses of codein and morphin for the alleviation of the pain. On February 1 diplopia appeared, with paresis of the right external rectus muscle. The pain was still severe and was localized in the temple and brow.

Examination (February 2). Pain is still severe and persistent; it is sharp and boring in character in the right temporal region, and there is complete paralysis of the right external rectus. All the other cranial nerves, including the optic nerves, are normal. Pupils are equal and react to light and accommodation. The corneal and conjunctival reflexes are present and equal on the two sides. No tenderness over the points of exit of the fifth nerve, and the sensation of the face is normal. Motor power and sensation of the extremities are normal. The tendon reflexes of the arms and legs are present and equal on the two sides. Skin reflexes are present. No Babinski. Heart and lungs are normal. The urine is normal. Rhinological examination shows no evidences of sinus disease. The Wassermann test is negative.

February 7. Has had almost continuous pain in the right side of the forehead, temple, and eye, requiring morphin. Pain of late has manifested a tendency to settle in the depths of the right eye, and there is marked photophobia. Complete abducens palsy on the right side persists, otherwise a general neurological examination is negative. On February 8 the pain shifted to the trigeminal area on the right side and is felt in the teeth and gums. After this the pain gradually moderated from day to day, and at the end of two weeks had completely disappeared. On April 1 she returned to her work. There is still paresis of the right external rectus, and she wears a ground glass to counteract the diplopia. She has had only one slight temporal headache since the last examination.

A few weeks later the diplopia disappeared, with complete restoration of function in the paralyzed rectus muscles.

October 14, 1914. She has continued her occupation and has never had any return of headaches or diplopia. The vision and ocular excursions are normal.

CASE IV.—A sister of the above patient, unmarried and forty-five years of age, has likewise been a sufferer from migraine since early childhood. The attack begins with pain in the temple, which gradually extends over the whole head. There is usually nausea and vomiting, and the severest pain is localized in the temporal region. There are no paresthesiæ and no visual disturbances in the attacks, which usually occur at the time of the menstrual period. During the past year, like her sister, she had been subjected to a severe nervous strain, nursing her mother during a long illness, which terminated fatally.

The Attack. Early in October, 1911, she was seized with one of her usual headaches, beginning in the left temple. It was of unusual severity and persistence, and was accompanied by vomiting. After the paroxysm had lasted several days, double vision made its appearance, and an oculist was called in consultation, who found an isolated paralysis of the left external rectus muscle; the fundi were negative and the other muscular movements were not affected. She wore a ground glass to counteract the diplopia, which did not disappear until the following April. Recovery was complete. There has been no recurrence of the paralysis since. Periodical unilateral headaches still recur at intervals.

COMMENT. These cases are of unusual interest on account of the extreme rarity of this ocular complication, and because of its occurrence in two sisters, in both consequent upon a migraine paroxysm. Such a familial coincidence is, I believe, unique, and would speak for the joint inheritance of a highly specialized type of this disease or of some vascular anomaly. It is significant that both cases had passed the middle period of life and had reached the age when organic vascular changes are likely to appear. Under these conditions a certain vasular distribution which for many years had been subjected to periodical spasms, with only functional disturbances, might at last, because of diminished caliber or elasticity of the vessel wall, give rise to organic changes from too prolonged obstruction of the blood current. It is interesting to note that in addition to the age factor, both sisters had been subjected to unusual worry and strain consequent upon the illness and death of a parent. The exact localization of the lesion in such cases is difficult to determine. The theory of a neural origin finds most favor, caused either by pressure or traction from swelling of the surrounding parts or by prolonged spasm of the vasa nervorum with consecutive ischemic degenerative changes in the nerve.

Remarks on Ophthalmoplegic Migraine. Ophthalmoplegic migraine has occupied a definite place in medical literature since the original contributions of Moebius[16] and Charcot[5] to this subject. The periodical oculomotor palsies, as they were first termed by Moebius, are at the present time regarded by most writers as allied to if not identical with the *migraine ophthalmoplegique*, as described by Charcot.

Two clinical types of this affection are recognized by systematic writers: a recurrent or periodical ocular palsy followed by complete recovery, and periodic exacerbations of a preëxisting paralysis of some of the branches of the third nerve.

This latter type has usually been associated with some organic lesion of the nerve or near the nerve at the base of the brain. In the few autopsies of this condition which are on record a variety of pathological conditions have been found. In the Thomsen-Richter[26] case a fibrous sarcoma was found attached to the third nerve, while in that of Karplus,[14] a neurofibroma of the dura had caused pressure on the nerve from below. In the Weiss[31] case a granuloma nodule was demonstrated on the nerve. In a more recent pathological contribution to the subject by Shinoya[24] there was a history of periodical oculomotor palsy beginning at the age of six; between the attacks remnants of the palsy persisted. Postmortem examination showed a fibrous-like swelling on the right third nerve, situated just behind the posterior cerebral artery. In the discussion of this case, emphasis is placed upon the fact that the third nerve passes between two arteries in its course at the base of the brain, the posterior cerebral and the superior cerebellar and that this may account for the very curious predisposition of this nerve to such lesions. Harvey Cushing[7] has also called attention to the possibility of vascular pressure and constriction as a cause of the neural complications of migraine.

The oculomotor paralysis in such cases may be complete as in Case II of my series, the paralysis involving both the intrinsic and extrinsic muscular mechanism, or it may be limited to the external muscles, as in Case I. Cases have also been described (Oppenheim[18]) in which only the intrinsic muscular mechanism was affected with paralysis of the iris and ciliary muscles.

An isolated palsy of the trochlearis muscles following migraine may also occur and is excessively rare, only two cases are recorded in the entire literature of this subject (Luzenberger[15] and Bornstein[1]).

Isolated paralysis of the sixth nerve associated with migraine is second only in rarity to trochlearis palsy; such cases have been observed by de Schweinitz,[8] Veasey,[27] Omerod and Holmes-Spicer,[17] Brav,[4] Oppenheim,[19] and Bornstein.[2]

In the case recorded by de Schweinitz the first attack occurred in a child only one year old, suggesting the recurrent oculomotor palsies which so frequently begin in childhood. In Bornstein's case the paralysis appeared as late as the sixtieth year. In the case described by Brav, both the migraine and the subsequent sixth nerve paralysis were peculiar, in that recurrences were observed only after parturition.

Not only are isolated palsies of the individual ocular nerves described in this affection, but they may be present in all possible combinations, even to the extent of complete opthalmoplegia (Brissaud[3]). Paderstein[21] has observed a combined abducens and trochlearis palsy in a migrainous woman of twenty.

In Cases II, III, and IV of my series, the ocular palsy first made its appearance in the middle period of life and should therefore be regarded as an accidental paralytic complication, such as will be described later in other arterial distributions, and not as a true relapsing or recurrent ocular palsy of the type of Moebius. They are cases of migraine with opthalmoplegia, rather than ophthalmoplegic migraine.

III. Migraine and Permanent Hemianopsia.

Case V.—*Summary. A man aged forty-four years, had suffered from migraine since childhood; after a typical attack there developed a right homonymous hemianopsia, which persisted.*

History. Mr. G., aged forty-four years; contractor by occupation. His father died at the age of seventy-nine years of a paralytic stroke; his mother is still living. There is no history of migraine in the family. He denies any venereal infection, and is the father of seven healthy children.

When two years of age he received an injury to the head, fracturing the frontal bone. There is still a slight depression in the frontal region, the result of this injury. Soon after this he developed epileptic seizures, which persisted to the age of six, after which time he had no subsequent attacks. At the age of thirty he received an injury to the right eye, which left a slight haziness of the cornea. From childhood he has been subject to typical attacks of migraine. These were severe up to his thirtieth year, after which they diminished somewhat in intensity. With the attack there is sometimes, but not always, a visual aura (lights and colors). The attack is usually accompanied by nausea, and frequently terminates in vomiting. He states that on a few occasions during the height of the pain paroxysm he seemed to loose consciousness, which he attributes to the agonizing intensity of the pain. He has noticed during the past year that in the attack or immediately preceding it the right hand becomes heavy and numb. This lasts for about fifteen minutes. There was no aphasia.

The Attack. On October 24, 1905, he was seized with one of his usual headaches. It was very severe, and, as was usual under these conditions, he went to bed. On awaking the following morning he was free from pain, but vision was very hazy and indistinct. He thought it must be still dark. Gradually during the day the vision improved, but there remained a persistent defect in the right visual field. He had no paralysis; no paresthesia, and no speech disturbance.

Examination (February 8, 1906). The pupils are equal, the left somewhat wider than the right. The reactions are perfect to both light and accommodation. No nystagmus. Opacities are visible in the left cornea. There is no paralysis of any of the cranial nerves, and the movements of the extremities are normal. The general sensibility is unimpared. The tendon reflexes of the arms and legs are present but more active on the right side. There is no Babinski.

The fields of vision show a partial homonymous hemiopic defect on the right side. The hemiopic pupillary reaction is not demonstrable. The optic disks are normal. In the blind area the sensation is not one of darkness but simply the absence of visual perceptions.

The heart is free from murmurs and the muscular tone is of good quality. No accentuation of the second aortic. Pulse is regular and soft. The urine is free from albumin or sugar. (Note: A written communication received from the patient in 1910, four years subsequent to this examination, states that the half-blindness still persists and that he is occasionally subject to attacks of migraine, although much less frequent and severe.)

Comment. The character and periodicity of the headaches in this case are typical of migraine. For one year previous to the development of hemianopsia he had noted during the attack a transient sensation of numbness and heaviness in the right hand which had never occurred previous to this time, and may well be construed as a warning symptom of the subsequent vascular lesion. Immediately following a typical attack he awakened to find the hemiopic defect in the right field of vision which has persisted. This was the only residual symptom of the attack, and indicates a lesion of the visual mechanism in its course behind the optic chiasm. As there was no haziness or darkness in the blind area, as usually occurs in lesions of the optic tract and chiasm, it may be assumed that the lesion was posterior to the primary optical centres, probably in or near the cortical area for vision. The absence of the hemiopic pupillary phenomenon is also in favor of a central and not a peripheral localization of the injury. The manner of development is strongly suggestive of thrombosis, although a hemorrhage cannot entirely be excluded. Such an attack must be directly attributed to the explosive disturbances of vasomotor function which occur in migraine. It is probable, however, that beginning vascular degenerations were of importance as a predisposing factor.

CASE VI.—*Summary. Severe migraine since childhood; at the age of forty-five, during an attack, developed a left homonymous hemianopsia lasting ten days, followed by recovery; eight months later a second attack, which was persistent; mitral disease.*

History. Patient is a woman, aged forty-five years; married; has had two miscarriages; no children. Her mother and two sisters have migraine. No history of epilepsy. Since childhood she has been subject to periodical attacks of hemicrania. The attack usually begins with vertigo. Pain is localized over the left brow and temple, and when severe may last two or three days. Occasionally the pain passes into the eyes and the bridge of the nose. There is usually nausea (churning sensations), but no actual vomiting. The attack occurs, as a rule, once a month, usually at the menstrual period. Often during the paroxysm the three ulnar fingers of the right hand become numb, but there is no weakness and no aphasia. Toward the end of the seizure she often sees bright lights of bizarre and striking form (scintillating scotoma).

The Attack. On March 9, 1906, during a severe attack, which had begun in the usual manner, there occurred a blurring of the left field of vision, which lasted ten days and then gradually faded away. Periodical headaches continued regularly after this attack, and were accompanied by numbness in the fingers of the right hand and a sensation as if the sight were going. Between the attacks she felt well and the vision was normal.

Second Attack. On October 27, 1907, she had a terrific headache; the pain was localized in the occipital region, and extended over the vertex into the eyes and the bridge of the nose. There was dizziness and nausea. In the attack a left-sided blindness appeared which has persisted up to the present time.

Examination (November 22, 1907). Pupils are unequal, the left being wider than the right; they react to light and accommodation. Fundi are normal. The cranial nerves are negative. The general motility and sensations are undisturbed. No Babinski. There is a well-marked homonymous defect in the left fields of vision. Heart: A musical, systolic murmur at the apex with hypertrophy of the left ventricle (mitral regurgitation).

Note: The hemianopic defect was still present in January, 1909, and she still suffers occasionally with headaches, which are less severe.

COMMENT. This case bears a close resemblance to the preceding one. Both patients were in the fourth decennium of life, and had suffered from migraine since childhood. In the first case the warning symptoms during the attack consisted of paresthesiæ and heaviness of the hand, while in the second the permanent hemianopsia had been preceded by transient attacks, one of which had lasted ten days. As mitral disease was present in this case, the question of embolism of the occipital branch of the posterior cerebral artery was considered, but finally discarded in favor of thrombosis because of the preliminary attacks of threatened occlusion, and also because of the etiological relationship between the migraine paroxysm and the organic defect, both of which favoring the probability of thrombosis.

Permanent hemianopsia following migraine is fortunately a rare complication. The residual defect may be a complete homonymous hemianopsia or a partial loss only may result, as in Case V of my series. This danger of the so-called ophthalmic migraine was originally emphasized by Charcot, and cases illustrating such permanent visual defects have been described by Charcot,[6] Féré,[9] and von Schroeder.[28]

In this country the subject has been presented in an able monograph by Dr. J. J. Thomas,[25] of Boston, who has personally observed three cases. In his observations, in addition to the hemiopic defect, there was associated a moderate degree of hemiplegia. T. A. Williams[32] has also recorded an interesting observation, in which migraine with hemiopic scotoma as an aura finally terminated in permanent hemianopsia.

IV. MIGRAINE AND HEMIPLEGIA.

CASE VI.—The patient is a single woman, aged thirty-two years, who had been subject to migraine since childhood. Her mother and other members of the mother's family have also been victims of this malady. The attacks are typical in nature, the pain being most severe in the occipital region, and usually terminate with nausea and vomiting.

The Attack. Early in August, 1912, while travelling, she was seized with a severe occipital headache of usual character, which terminated in vomiting. A physician was called and she was given hypodermics of morphin to relieve the pain. The following day the headache was better, and in the course of a week she had regained her usual health. Three weeks later she had another severe attack of pain in the occipital region, which likewise came on while travelling. She got up in the night in order to vomit and fainted. On arriving in New York she was taken to the New York Hospital in a semiconscious state.

Examination (September 7, 1912). She is semiconscious and can be aroused with difficulty, but immediately relapses into stupor. There is slight stiffness of the neck and a distinct paresis of the left arm and leg, with a corresponding weakness of the left face. The tongue deviates toward the left. The abdominal reflexes are absent on the left side and the Babinski is present on both sides. No paralysis of the cranial nerves. The heart is free from murmurs. The pulse is rapid and the respirations are increased in frequency and at times irregular. Lumbar puncture shows the presence of fresh blood. This was repeated on four other occasions, and always with the same result. The Wassermann test of the blood and cerebrospinal fluid was negative. Blood cultures and cultures of cerebrospinal fluid were also negative. The urine was normal. There was a leukocytosis of 16,000, with 86 per cent. polynuclears. Examination of the nasal sinuses was negative.

At the end of twenty-four hours the stuporous condition diminished and was replaced by a restless delirium. She had at no time any convulsive seizures. As the mental condition improved it was noted that in addition to the left hemiplegia there was also hemianopsia upon the left side. At this time an ophthalmic examination showed a slight degree of optic neuritis, a little more pronounced in the right than in the left eye.

Her mental condition gradually cleared and the hemiplegia and hemianopsia gradually diminished and she eventually made a complete recovery.

COMMENT. The diagnosis in this case was at the time and still is somewhat doubtful. The complete recovery is in favor of a vascular lesion. There is no question as to the existence of migraine in this patient, and of a strong family tendency to this disease. There seems also very little doubt that the apoplectiform seizure was the culmination of a severe migrainous paroxysm, and while there may have been some preëxisting vascular or other organic defect of the brain structure, the determining rôle played by the migraine explosion seems to have been a perfectly definite one.

Cases of migraine which have terminated in hemiplegia have been described by Féré,[10] von Schroeder,[28] Oppenheim,[20] and Infeld.[29]

Oppenheim's case was that of a woman who had suffered from migraine since childhood. Four months after giving birth to a child she had an attack of migraine with aphasia, which cleared up in twenty-four hours. She subsequently had four similar attacks of transient aphasia, all occurring after paroxysms of migraine. In the last attack there was aphasia and a right hemiplegia with delirium which terminated fatally. The autopsy showed an area of softening in the left cerebral hemisphere, produced by thrombosis of the left internal carotid near the origin of the Sylvian artery. Microscopically, the vessel wall showed a distinct endarteritis, with thickening of the adventitia, so that in this case there was evidently a preëxisting organic defect in the vessel wall which could not withstand the acute vascular disturbances consequent upon an attack of migraine; and while migraine was by no means the sole cause of the accident, it was a strongly determining factor.

Von Schroeder has described a somewhat similar case in a man, aged thirty years, who had been subject to attacks of ophthalmic migraine since his twentieth year. Following a series of severe attacks, all typical in their manifestations, he suddenly lost consciousness and developed a left hemiplegia. On recovering consciousness he was found to have in addition to the paralysis a left hemianopsia. The hemiplegia improved but the hemianopsia persisted as a permanent defect.

Infeld has also described the case of a woman, aged twenty-nine years, a sufferer from migraine since her twelfth year. Following a migraine paroxysm she developed a right hemiplegia which gradually improved but left in its wake persistent weakness, paresthesiæ, and athetosis of the right hand.

V. Migraine and Lesions of the Optic Nerve.

Summary: A woman, aged thirty-one years, subject to migrainous seizures since childhood; after a severe attack she developed a unilateral retrobulbar neuritis with paracentral scotoma; recovery.

History. The patient is a woman, aged thirty-one years; single; for many years under my care for migraine and various neurasthenic symptoms. She has been almost completely deaf since her fifteenth year (otosclerosis). She has also a congenital ocular palsy, involving the left external and both internal recti muscles. A brother and one sister have also congenital defects of the ocular muscles. As her deafness progressed she became suspicious, irritable, and peculiar, and at the age of twenty-five developed a delusional state with ideas of persecution, from which she recovered in the course of a few months. Since her thirteenth year she has been subject to typical attacks of migraine, with scotoma and vomiting. After the twenty-first year these attacks have recurred periodically, but are much milder in character. They begin in one temple and gradually become diffused over the entire head.

The Attack. On February 18, 1912, she had a severe migrainous seizure, beginning in the right temple and rapidly extending over the entire head. Pain was especially excruciating in the region of the right temple, and radiating into the right eye. To relieve this pain she took during the course of the night 20 grains of pyramidon in divided doses. In the night she vomited, after which she felt somewhat better and fell asleep. The following morning (February 19) on awaking, she found the vision in the right eye was hazy and blurred, and as if looking through a veil. The vision in the left eye was perfectly normal. The movements of the right eye were slightly painful and the eyeball somewhat tender to pressure.

Dr. J. Wolf made an ophthalmoscopic examination at this time and found a slight congestion and haziness of the right optic nerve. The right field of vision showed a relative scotoma in the centre and to the temporal side of the fixation-point (paracentral scotoma). Vision: O. D., 15/15.

February 22. Can scarcely count fingers with right eye. Eyeball still slightly tender.

March 4. Vision is showing some improvement.

March 7. Vision: O. D., 15/20. Still paracentral scotoma.

April 19. Central vision normal. The acuity of the periphery is still somewhat diminished (veiled), but the peripheral limits of vision are normal. In the right eye there is a very faint pallor of the optic nerve. Diagnosis retrobulbar neuritis. The rhinological examination, including illumination of the sinuses, was also found negative (Dr. J. Wolf). Roentgenogram of the sinuses showed no pathological changes.

The urine is normal; heart is normal.

COMMENT. This case is recorded because of the apparent relationship of unilateral retrobulbar neuritis to a migraine paroxysm. Such a sequel is not recognized by systematic writers on this subject.

Oppenheim,[19] however, states that he "once observed a patient with migraine who developed an optic neuritis with paracentral scotoma, and although the causal relationship may be doubtful, it is well to bear in mind the probability of such a complication."

Other migraine complications referable to the optic nerve are, however, definitely recognized. For example, Voss[30] has observed unilateral optic atrophy after the attack in a woman who had reached her forty-second year. She had been subject to hemicrania since childhood, and following a severe attack became suddenly blind in one eye. This was caused either by hemorrhage into the optic sheath or thrombosis of the central artery of the retina. Galezowski[12] has also observed thrombosis of the central artery of the retina from a similar cause. In this connection it is of interest to note that hemorrhages into the retina and detachments of the retinal membrane have occurred during the migraine paroxysm.

VI. CONCLUDING REMARKS.

Without reviewing in detail, all the theories which have been formulated in explanation of the symptomatology of genuine migraine, it may be assumed that there is periodical recurrence of an autointoxication, the chief effects of which are experienced by the sympathetic and vascular systems. As a result of this there is induced a condition of more or less localized vasomotor spasm or vasomotor dilatation of the cerebral circulation (angiospastic and angioparalytic types of migraine).

Some idea of the degree of vasomotor disturbance to which the cerebral vessels are subjected may be surmised from the results of opthalmoscopical examination of the retinal circulation during the attack. At such times there has been frequently noted a marked pallor of the optic nerve and retina, from contraction of the vessels, which gradually disappears with the subsidence of the seizure. The fluctuations in the size of the temporal artery during the paroxysm is so well known as scarcely to require mention.

It would seem reasonably safe to assume that what occurs in the distribution of the ophthalmic and temporal arteries may also occur in other regions of the cerebral circulation, and this vascular spasm is regarded by most observers as the cause underlying the transient focal symptoms so frequently associated with this disease, viz., scotomata, paresthesiæ, paresis of the extremities, and aphasia, all of which disappear with the subsidence of the spasm.

Another important and interesting question is the etiological relationship of hemicrania to premature cerebral arteriosclerosis. Some writers maintain that the frequent recurrence of vascular explosions in migraine over a period of many years are in themselves sufficient to cause cerebral arteriosclerosis. The auto-intoxication which is the underlying basis of the disease is also recognized as a probable contributing factor.

Of great importance from the stand-point of the permanent sequelæ such as are described in this paper is the question of the influence of recurring attacks of migraine upon an already existing arterial sclerosis. It is very evident that in the presence of cerebral arteriosclerosis, however slight, that crises of hemicrania are much more likely to be the cause of vascular accidents, such as thrombosis and hemorrhage than would be the case in perfectly normal vessels. It is this combination of factors which would appear to be the important one in many of the cases which have just been described.

Another element which must be considered is the possibility of arterial anomalies in the blood supply of the brain and cranial nerves which might render a certain arterial distribution especially vulnerable in the event of sudden vascular spasm.

In the recognition of migraine paralysis the essential points to be considered are: (1) the establishment of a definite clinical history of genuine or idiopathic migraine, and (2) the direct relationship of the paralysis or other complication to the migraine paroxysm. As many attacks of hemicrania begin during the day, terminating in a heavy sleep, the presence of paralysis in the morning on awakening would be strong presumptive evidence of an etiological relationship to migraine. Special emphasis should also be placed upon the presence of what may be termed "warning symptoms," *i. e.*, the recurrence of transient ptosis, diplopia, hemianopsia, hemiparesis, aphasia, and Jacksonian seizures, when such symptoms appear in middle life after a migraine paroxysm. Especially significant are such symptoms when they are foreign to the usual attack. For example, a migraine accompanied or preceded by transient hemianopsia, when this has been an early and more or less constant phenomena of the attack, would not have the same importance as when this symptom appears suddenly in middle life out of a clear sky. On the other hand, it must be recognized that in just such cases with recurrent scotomata the danger of permanent hemianopsia is by no means a slight one.

A permanent damage to nerve structure following an attack of migraine is fortunately a rare sequel. In this group of accidents the ocular palsies rank first in importance, because of their relative frequency (migraine ophthalmoplegique). Flatau[11] in his comprehensive study of the subject has collected and analyzed 97 such cases.

Next in importance among the cranial nerve complications is the involvement of the optic nerve, *e. g.*, by thrombotic occlusion of the central artery of the retina, and possibly retrobulbar neuritis.

An importance is attached by some writers to the very doubtful association of migraine with facial paralysis (the so-called hemicrania facioplegica). This is based upon the contribution of Rossolimo,[22] who described a relapsing facial palsy in conjunction with migraine. This case stands alone in literature and, therefore, naturally awakens the suspicion of a mere coincidence, namely, the accidental association of migraine with relapsing facial palsy. It is well known that attacks of recurrent facial paralysis are by no means rare, and Bernhardt has placed the percentage as high as 7.2 per cent. of all cases of Bell's palsy. When it is still further considered that pain in the mastoid and occipital region often very severe and persistent, is one of the common symptoms of facial paralysis because of the sensory system of the facial nerve (Hunt[13]) it is evident that the pain of migraine may be closely simulated. Certainly at the present time there is no just ground for recognizing a clinical type of facioplegic migraine in the sense that we accept the *migraine ophthalmoplegique* of Moebius and Charcot.

In passing, it is of interest to recall the observation of Sil,[23] who noted a transient paresis of the hypoglossal nerve in a case of ophthalmoplegic migraine. This observation, like that of Rossolimo, is unique and in no sense constitutes a definite clinical type.

The graver paralytic complications are naturally those affecting the brain itself, and these are the result of occlusion of the cerebral vessels with consequent encephalomalacia. Such lesions have been observed in the distribution of the Sylvian artery causing hemiplegia, hemi-anesthesia, and aphasia, and in the distribution of the posterior cerebral artery when homonymous hemianopsia is the characteristic symptom. While thrombosis is the usual lesion in such cases, it is not improbable that rupture of the vessel sometimes occurs.

I am not aware of any permanent sequelæ, after an attack of migraine, which could be traced to occlusion of the vessels of the pons, medulla or the cerebellum. This is rather curious and difficult of explanation, considering the rich blood supply in this region and its frequent involvement from other causes.

It is of interest to recall that Oppenheim has described a cerebellar type of migraine in which, with the general symptoms of this disease, there were transient symptoms of cerebellar origin; so that the possibility of permanent vascular lesions of the brain stem and cerebellum having this origin, must be kept in mind.

There are two other groups of cases which should be considered from the stand-point of permanent vascular lesions, namely, the epilepsy which is so often associated with migraine and the *vertigo permanens.* Both of these conditions are usually regarded as merely functional substitutions or alternations of the neurosis itself, in other words, as a kind of migraine equivalent. And while I am heartily in accord with this hypothesis, the possibility of a permanent vascular focus resulting from an attack of migraine must be considered as a possible etiological factor in the presence of either epilepsy or persistent vertigo.

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THE ROENTGEN-RAY IN GASTRO-INTESTINAL AFFECTIONS.[1]

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In reviewing the literature on roentgenology, one recognizes that for a number of years most of the advancements in this specialty have come from the same contributors. The men who are maintaining high standards of work are few, and as a consequence the physician is often obliged to accept the interpretations of inadequately prepared roentgenologists. The apparent simplicity of this science has caused a number of men to follow it who have not the necessary preliminary training to properly qualify them for their work.

The subject is new, and its literature, particularly in English, is so scant that one who is seeking to perfect himself in this specialty is able to find but few reliable sources of information. The isolated observations and occasional monographs are not always readily accessible. The courses offered for the study of roentgenology in both graduate and undergraduate schools are limited, and the amount of time that can be devoted to the subject by the undergraduate is restricted. The average postgraduate schools do not give the thorough training which is so much to be desired, because the time allotted is too short and the number of cases completely studied far too few.

There is a lack of uniformity in the methods of roentgenological examination followed by specialists of apparently equal standing.

[1] Read before the annual meeting of the American Gastro-enterological Association at Baltimore, Md., May 10, 1915.

To illustrate: there is no standard or test meal for roentgenographical examination of the gastro-intestinal tract. The American, German, and English test meals differ. Such a standard meal is as necessary for roentgenographical examination as the Ewald test breakfast for chemical analyses. A standard test meal would obviate the necessity of always specifying which opaque salt was used.

Physicians without sufficient experience in roentgenology often draw erroneous conclusions, and their patients are frequently subjected to improper treatment because diagnoses are made from incomplete roentgenographical findings, based on too few plates or a hasty fluoroscopical examination. Such inaccurate examinations are allowed to displace the ordinary routine diagnostic methods, and, as a frequent result, the patient is treated medically or surgically for a condition that does not exist.

An accurate knowledge of the pathology that is subject to roentgenological examination is necessary for decisive interpretations. Time and again it has been emphasized that the skilled roentgenologist must be a good clinician, one who is able to correlate the clinical history and the present physical condition of the patient with the laboratory findings. That a roentgenologist should have a thorough training in pathology has not been heretofore emphasized. If one is unable, through insufficient knowledge of pathology, to form an adequate mental picture of the physical changes resulting from disease, he cannot understand the records shown on the Roentgen plate. The Roentgen-ray may be likened to a most powerful microscope, revealing living structures in health and disease. Just as it is necessary to have an accurate knowledge of histology and pathology in order to interpret a cut section of tissue, so it is imperative that our roentgenologists should be grounded in anatomy, physiology, and pathology if they are to make their conclusions valuable and decisive to the consulting physician. Few clinicians have sufficient knowledge of Roentgen pathology to justify them in attempting the full interpretation of a series of plates.

The Roentgen-ray diagnosis of pronounced gastric pathology is comparatively easy. Definite lesions, which are conspicuous at autopsy or operation, are readily recognized. The recognition of an hour-glass stomach, a perforating ulcer of the stomach, or an obstruction of the pylorus is not very difficult. The statement has been made that fully 95 per cent. of patients with so-called stomach symptoms are not really suffering from gastric disease but from some other abdominal disease, as chronic appendicitis or cholecystitis. The roentgenologist should therefore have the special training that is necessary to enable him to discover by the Roentgen-ray the remote lesion that is the cause of the patient's symptoms. These cases of reflex irritation in which the pathological condition may be in the gall-bladder, in the appendix, or in the colon, offer the roentgenologist his most difficult problem and an opportunity to show his experience and the refinement of his technique.

In order that the limitations and possibilities of Roentgen diagnosis may be established, it is necessary to secure a standardization of methods and technique.

Many cases have been observed which illustrate the need of a universal technique. I will quote one typical case, in which the roentgenologists concerned, leaders in this specialty in different cities, because of variation in technique, reached different conclusions. The point involved was the position of the stomach. One roentgenologist reported that with the patient in the prone position the stomach was drawn upward and to the right of the median line, indicating the so-called "gall-bladder position." The second roentgenologist independently reported as follows:

"It is to be understood that I had no knowledge of the first examinations until my conclusions were complete. If the patient is examined in the upright position, I question whether such roentgenograms as Dr. X. shows could be obtained, as in my whole series with the patient in the upright position, not only by plate but by fluoroscopy, the stomach swings well to the left of the median line and by manipulation is apparently in no way fixed. I have found by experience, whether it be true or not, that a patient studied by the fluoroscope in the prone position, such as Dr. X. refers to in his report, leads to just such conclusions as he has reached. This is due in a great measure to pressure which is to be expected in well-nourished individuals."

The question involved, a matter of position is a simple one, but because of the slight difference in technique the positive diagnosis of one examiner was discredited by the second on the basis that the observations upon which the first diagnosis was made were due to the position of the patient at the time of the examination. It is evident that a definite and uniform plan of procedure in Roentgen-ray work must be adopted if the conclusions of the roentgenologists are to be respected.

We must always remember that the stomach is a flexible, muscular organ, capable of widely different appearance when viewed with slightly varying technique under slightly differing conditions.

Roentgenologists are constantly being asked what machines to buy. A prominent roentgenologist states that he is almost daily in receipt of letters inquiring about the kind of a machine to purchase. More emphasis is often placed upon the choice of a machine than upon the acquirement of the knowledge necessary to enable one to interpret the diagnostic data produced by the machine.

As an example of incorrect diagnoses produced by embryonic roentgenologists, we would cite the following: A physician was induced by a persuasive agent to purchase a powerful Roentgen-ray machine. He took six 14 x 17 plates of six different cases, *i. e.*, one of each case, and advised surgical operation in every case.

This man, on account of his inexperience, did not know the normal roentgenographic appearance of the human gastro-intestinal tract. The six patients underwent operation, and in none of them was any pathological condition found in the abdomen. One of the cases showed a normal stomach with two peristaltic waves present. The portion of the stomach included between these waves was diagnosed as a neoplasm, and operation was advised on the strength of this diagnosis. It seems incredible that a physician without adequate training and experience in roentgenology should assume the responsibility of advising such serious surgical procedure.

A prominent surgeon in a large hospital bought a roentgenographic apparatus and undertook roentgenography. His first case was a typical hour-glass stomach, which showed very well on the single plate taken. The easy diagnosis of this comparatively simple condition greatly encouraged him to continue. Then followed a series of cases, each diagnosed from a single plate. The percentage of errors which necessarily followed was very high.

A few cases will be cited to illustrate and emphasize points previously mentioned. The first is that of a man, aged thirty-eight years, whose chief complaint was loss of weight. The roentgenologist found a slight filling defect in the transverse colon to the right of the median line. Only one examination was made. Operation for carcinoma was advised. At operation the colon was found to be normal. This roentgenologist did not make a sufficient number of plates, and did not know that the filling defect he observed is a normal finding. Since spastic manifestations may be due to various causes, we feel that no surgical intervention should be advised on a single examination.

A patient, aged thirty-five years, whose complaint was indigestion, was carefully examined by an internist, who thought he detected free fluid in the abdominal cavity. An aspiration was done and a few cubic centimeters of bloody serum secured. The patient consulted a surgeon, who, after an examination, decided that the case was one of gastric carcinoma, and desired the opinion of the roentgenologist. The surgeon had been accustomed, just before sending such cases to his roentgenologist, to invariably give them a gastric lavage. The fluoroscopic and roentgenographic examinations showed a pyloric filling defect in all the plates. A diagnosis of carcinoma was made, and agreed to by the internist and surgeon concerned. One month later the roentgenologist saw the man, who had gained in weight and was feeling very well. He realized at once that he had erred in his diagnosis and closely questioned the patient. He discovered that one-half hour previous to his roentgenographic examination the patient had eaten a hearty meal and that he had not received the usual gastric lavage. These facts easily explained the appearance of the filling defect and the consequent error in diagnosis. The man is alive and well today.

We have record of at least ten cases of deformity of the duodenal cap in which a diagnosis of ulcer was made by roentgenography, surgery advised, and at operation a chronic appendicitis found. Such cases of apparent deformity belonging to the group of "spastic contractions" are prevalent and require diagnostic skill to distinguish them from actual lesions of the pylorus and duodenum.

A series of eight cases in which a diagnosis of gastric or duodenal ulcer was made, based upon a careful Roentgen-ray examination, is most interesting and instructive. At operation no pathology of the stomach or duodenum was found. The appendix was removed in all these cases and the gall-bladder inspected. The patients obtained no relief from their symptoms, and at subsequent operations, performed within one year, definite gastric or duodenal ulcers were found. The surgeon simply explored the peritoneal surface at the first operation and therefore failed to find the lesions demonstrated by the Roentgen-ray. These cases illustrate that the surgeon and clinician should be slow to discredit the diagnosis of the well-trained roentgenologist.

The welfare of the patient is best served by the friendly team work of the internist, surgeon, and roentgenologist. This necessitates a careful review and correlation of the findings of each of these specialties. An antagonistic and hypercritical attitude of the respective physicians concerned often retards the diagnosis.

I am of the opinion that the adoption of certain recommendations will increase the value of the Roentgen-ray as a diagnostic aid in gastroenterology. I do not offer these suggestions in a spirit of criticism, but am prompted by a desire to secure better coöperation between clinicians and roentgenologists. These recommendations are:

1. That the roentgenologist should be a trained and experienced anatomist and pathologist.
2. That there should be standardization of methods and technique.
3. That the physician acquire the ability to properly estimate the diagnostic value of a Roentgen-ray report.
4. That the patient should not be subjected to operation without a confirmation of the original findings by a second Roentgen examination made after an interval of two or three days.
5. That the clinician must not attach too much significance to the Roentgen-ray findings unless they are absolutely decisive.
6. That the lesion discovered by the Roentgen-ray must be a constant finding, regardless of position or slight variations in technique.
7. That great care must be exercised to differentiate physiological and spastic conditions from those that are essentially pathological.
8. That the Roentgen-ray report should be considered on the same basis as any laboratory report.
9. That the physician must carefully correlate the Roentgen-ray findings with the anamnesis and the clinical and laboratory findings.

THE LATE RESULTS OF CARDIORRHAPHY: REPORT OF CASE THREE YEARS AFTER OPERATION.

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NEW YORK.

Although the immediate results of cardiorrhaphy have been brilliant, as is attested by the fact that approximately 50 per cent. of patients have recovered after operation, according to the statistics of E. Hesse, Müller, Wagner, and others, a feeling of uncertainty must exist as to the ultimate condition of these patients. The question naturally arises as to whether an individual whose heart has been wounded, subsequently exposed by operation, handled and sutured, can return to the same condition of health as before. It is important for the future of cardiac surgery that the effects of such traumatism upon the action of the heart and upon the health and working capacity of the patient should be determined. With this in view we report the late results of a case of cardiorrhaphy operated upon by one of us three years ago, and likewise present the late results of similar cases in so far as these could be ascertained.

Case Report. On July 18, 1911, a young man, aged twenty-four years, was brought to the New York Hospital about thirty minutes after he had stabbed himself with a knife. The patient was in a condition of profound shock. There was a wound about one-half inch in length in the fourth intercostal space close to the upper border of the fifth rib and just mesial to the nipple. From the symptoms and physical signs it seemed reasonably certain that there was a wound of the heart. Accordingly operation was undertaken without delay. The following description of the operation and post-operative course is taken from the *Annals of Surgery*, 1912, lv, 485:

"The wound was extended along the upper border of the fifth rib toward the sternum, crossing and dividing the cartilage near its insertion. The stab wound entered the pleura, and in exposing the pericardium the pleura was injured further. The pericardium was incised in the direction of the wound, allowing the escape of considerable blood, and the index finger was inserted into the pericardial sac. It failed to locate the wound in the heart, but palpation of the inner surface of the pericardium revealed an opening in it, corresponding in position to the original surface wound. The exposure of the heart was rapidly improved by making a 'trap door.' For this the incision was carried upward along the sternum and thence outward along the lower margin of the third costal cartilage. The cartilages of the third and fourth ribs were divided close to the sternum, the third being readily exposed by retracting the soft parts upward. The two cartilages were then carefully lifted, separated from the pleura, and fractured at the costochondral junction, forming a flap with skin and muscles attached; resection of the fifth cartilage was contemplated but was delayed and did not prove necessary. The internal mammary was clamped and ligated above and below when exposed. The opening in the pericardium was enlarged by an incision upward near the sternum, making a triangular flap. Hemorrhage was very free.

Palpation revealed the rent in the heart, which admitted the tip of the index finger. As the finger was withdrawn from the hole a well-vaselined silk suture was passed from above downward on a fine curved intestinal needle; this was tied and left long. By gentle traction on this suture the heart was readily lifted and rotated, so that the wound was rendered visible and readily accessible. The wound involved the left margin of the heart somewhat posteriorly; it was about one-half inch in length, transverse on the long axis of the heart, and approximately one and one-half inches above the apex. Though the wound was partially closed by the first suture, blood gushed out whenever the finger was momentarily lifted to pass a stitch. Five stitches were inserted and tied before the bleeding was completely controlled. All visible blood was then removed and the pericardium closed with interrupted catgut stitches. There was considerable tension between the edges of the pericardial wound, which caused some gaping between the stitches in the lower mesial part. The flap was replaced and chromic stitches used to repair muscles and fascia. The skin was closed with silk. In the outer angles of the wound rubber tissue drains were inserted through the skin. At the lower mesial angle of the wound a rubber tissue drain was inserted down to but not into the pericardium. After the wound in the heart had been closed an infusion of 16 ounces of salt solution was given. The operation took about thirty minutes.

Post-operative Course. For twenty-four hours after the operation the patient was restless, irritable, and thirsty. He was given morphin freely and saline continuously by rectum (Murphy drip). During this time the highest pulse rate was 128; respirations were 24 to 28; temperature, 102°. When the dressing was changed at the end of sixteen hours and the drains removed, a very large quantity of clear serum exuded from the drainage openings. A rubber tissue drain was therefore reinserted at the lower inner angle. A similar discharge occurred again at the next dressing thirty hours after the operation. At that time the pulse had risen to 132; the temperature remained 102°. White blood cells were 19,000, polymorphonuclears, 83 per cent. The serous discharge continued to be free until forty-eight hours after the operation, when the single remaining drain was removed from the lower and inner angle of the wound. At this time the pulse was 112, temperature 101°, respirations 24. The patient was refractory and refused to eat, because, he said, he wanted to die; he was also very irritable and restless. Twice he sat up in bed. Morphin was given and he became quiet. Rectal alimentation was begun.

July 22 (fourth day). Condition good, pulse 104 to 124, temperature 102°. White blood cells 17,500, polymorphonuclears 84 per cent. Patient still refused nourishment. Wound dry and clean.

July 23. Condition about the same.

July 24 (sixth day). Large amount of serum exuded from the wound, after which the pulse became very rapid.

July 25 (seventh day). Constant free discharge of clear serous fluid requiring frequent dressings. The patient still refused nourishment, was extremely weak, and appeared to be in serious condition."

The systolic blood-pressure, taken twice a day from the third to the eighth day, was always between 90 and 110.

July 26 (eighth day). The patient was persuaded to eat by threats of passing a stomach tube; nutrient enemata were discontinued. Wound dry and clean, temperature normal, pulse 90, white blood cells 10,000, polymorphonuclears 74 per cent. From this time the convalescence was uneventful. He was allowed up on the eighteenth day and discharged from the hospital on the twenty-fifth day."

The man was imprisoned for two and a half years after leaving the hospital and followed the routine prison life without inconvenience; for the last six months he has led an active life.

On August 16, 1914, he reported for examination. He stated that on exertion he often experiences a dull pain in the region of the heart which lasts for a few minutes. Since the operation, he has had slight shortness of breath on walking fast or climbing stairs rapidly. Otherwise, his health and strength have been normal.

Physical Examination. The patient is well developed; of medium height; weighs 131 pounds (at time of injury, 129 pounds).

Chest: Size and shape normal. A large scar is present over the precordial area. The scar consists of three limbs. The upper transverse limb, measuring 4 cm., corresponds to the third intercostal space; the lower, 7 cm. long, corresponds to the fifth interspace. The vertical limb is close to the left border of the sternum. Respiratory movements are normal.

There is a systolic impulse diffused over an area about 4 cm. in diameter and with its maximum intensity about the centre of this area at a point 8 cm. to the left of the midline in the fifth interspace. A slight diastolic retraction can also be seen over this area.

Tactile fremitus is normal over entire chest. The cardiac impulse is felt with maximum intensity in the fifth interspace 8 cm. to the left of the middle line with patient in upright position; with patient lying on the right side it is felt 6.5 cm. from the midline, and with patient lying on the left side 11 cm. from the midline. No thrill felt.

Pulmonary resonance is normal over the entire chest. The right border of the heart percusses 1 cm. to the right of the right border of the sternum; the left border percusses 11 cm. to the left of the midline.

Respiratory sounds are normal over entire chest. No adventitious sounds are present. The first heart sound is heard with maximum intensity in the fifth interspace 8 cm. to the left of the midline. A soft blowing systolic murmur is heard with maximum intensity in the fifth interspace 8 cm. to the left of the midline and is transmitted for about 4 cm. to the left and 2 cm. to the right of the point of maximum intensity. No other murmurs heard. No friction rubs present. Muscular quality of heart sounds is good. The pulmonic second sound is slightly accentuated.

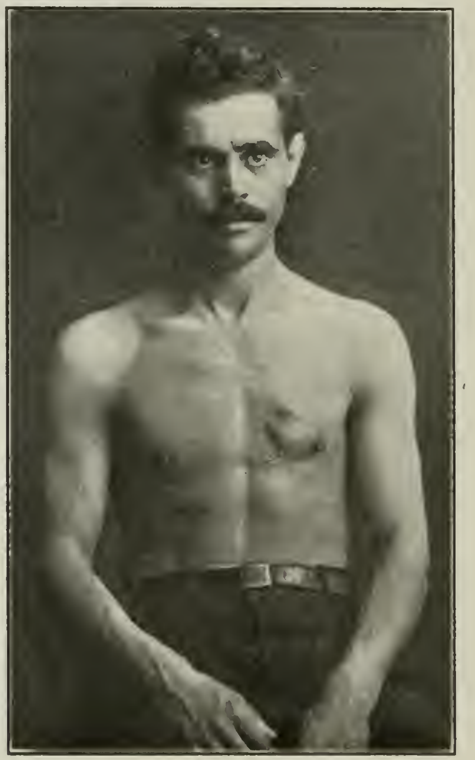

FIG. 1

Pulse: The pulse was 70, regular in force, volume, and rate. The blood-pressure while at rest is: left arm, 110 systolic, 60 diastolic; right arm, 112 systolic, 60 diastolic.

After active exercise with chest weights for five minutes the pulse rate is increased to 75 beats per minute, the blood-pressure

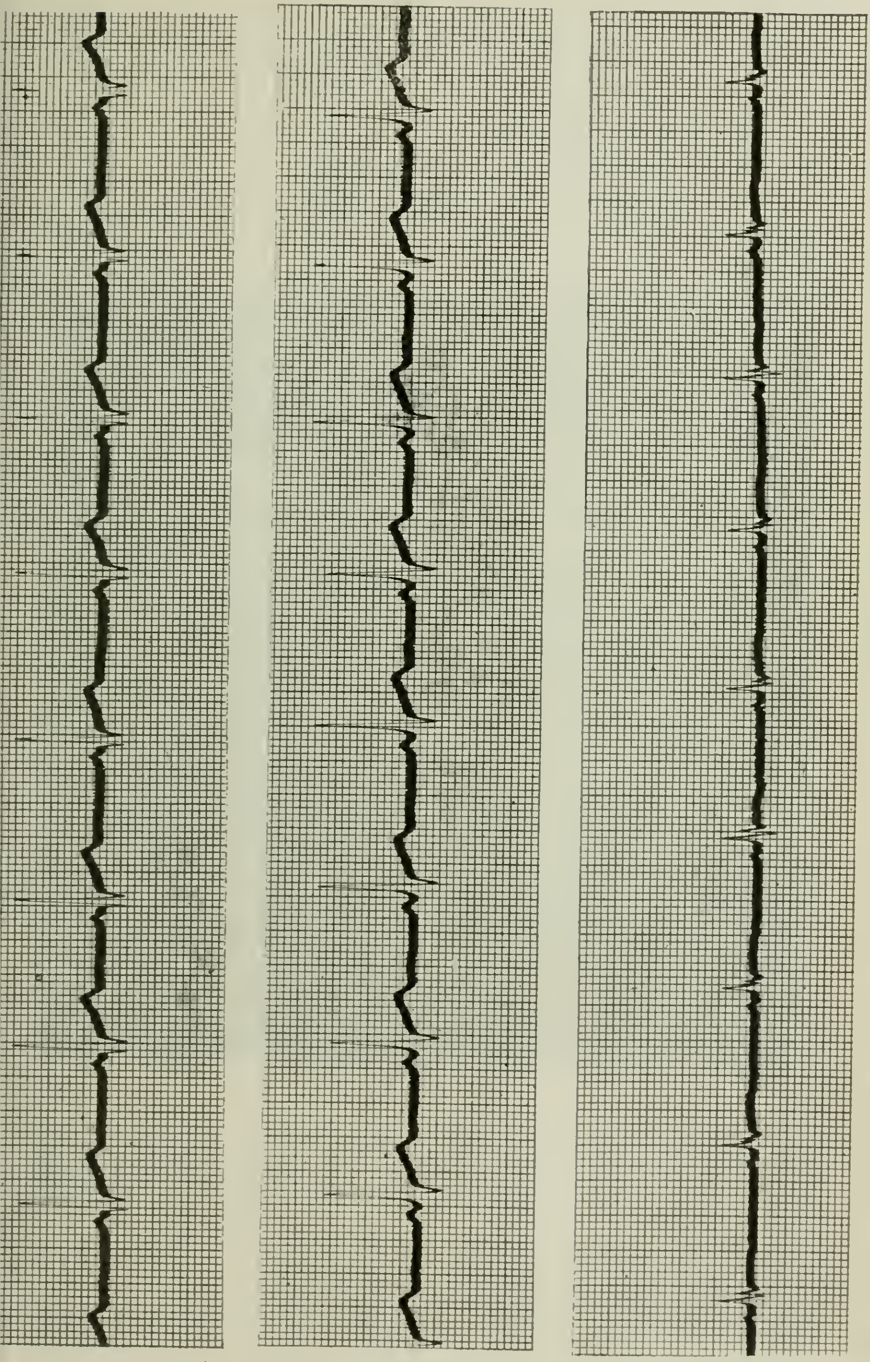

FIG. 2.—Upper curve from lead I, middle from lead II, and lower from lead III. Abscissa, 1 div. = 0.04 sec. Ordinate, 1 div. = 10.4 volt.

remaining the same; left arm 112 systolic, 60 diastolic; right arm, 112 systolic, 60 diastolic. After resting for five minutes the pulse rate is 70 per minute and the blood-pressure; 110 systolic, 60 diastolic in both arms.

The heart work (Sahli sphygmobolometer) is: 11.2 gm. cm. of Hg. left arm; 12.4 gm. cm. of Hg. right arm.

No abnormal venous or arterial pulsations visible; no visible capillary pulsations; no cyanosis, edema, nor pallor. The physical examination presents nothing further that is worthy of note.

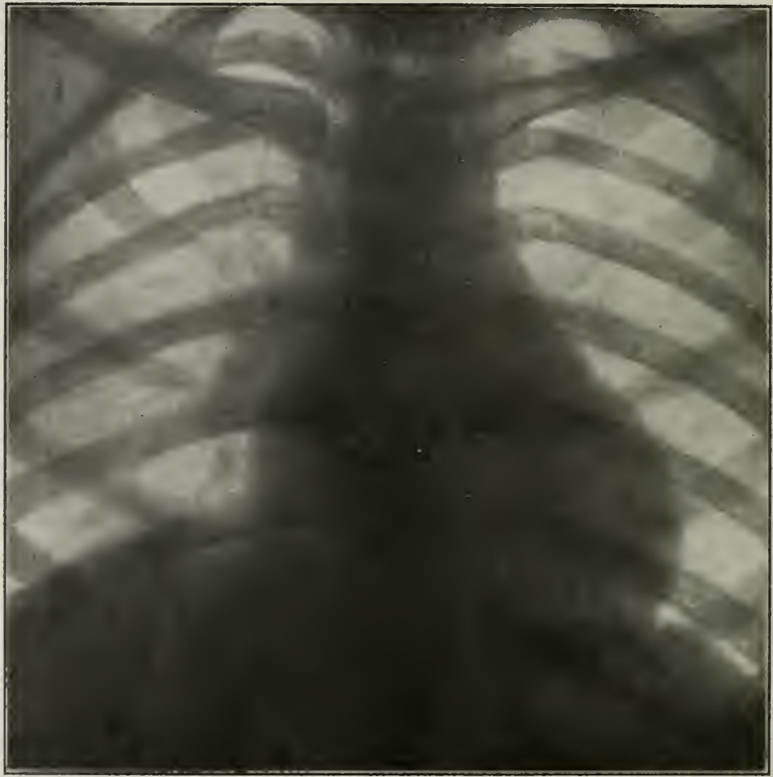

Fig. 3

An electrocardiogram (Fig. 2) (Dr. Horatio Williams) shows a normal curve with the exception of a slight retardation in the conduction time, which probably is not dependent upon the injury to the heart.

Simultaneous tracings taken at the apex, carotid, and jugular show normal curves. (MacKenzie polygraph).

Roentgen-ray examination (Fig. 3).

Dr. A. H. Busby: The heart appears to be normal in size, shape, and situation; it extends one inch to the right of the right margin of the sternum and three inches to the left of the left margin of the sternum, the widest horizontal measurement of the heart being five and three-quarter inches. There is no niche or indentation breaking the outline, and there is no suggestion of adhesion or distortion. The outline of the heart in the supine position is very clear. Enlarged lymph nodes are seen at the hilus of the lung and also about some of the larger bronchial ramifications.

The Late Results in Published Cases of Successful Cardiorrhaphy. An attempt has been made to ascertain and record the late results in the reported cases of recovery after heart suture. The facts about some of these cases were obtained through personal communications as a result of letters which were sent in January, 1913, to those surgeons who had reported successful cardiorrhaphies prior to 1912. The replies were relatively few and consequently the collection of ultimate results is not as complete or enlightening as could be desired.

Parlavecchio: Operation 1898. Male, aged twenty years. Stab wound in fifth left space. Eight hours between receipt of wound and operation. Resection of fifth rib. Wound in left ventricle near apex 3.5 cm. in length. Four silk sutures. No drainage of pleura or pericardium; no complications. Recovery.

The patient was seen in 1913, fifteen years after operation. His general condition was excellent. He is in the flower business and can work well. Local examination shows nothing abnormal except a systolic retraction at the cicatrix. (Personal communication.)

Launay: Operation, 1901. Pistol-shot wound at left nipple. Male, aged twenty-six years. Extreme hemothorax. Lung wounded. Four hours between receipt of wound and operation. Flap of fourth, fifth, and sixth ribs, hinge external, pleura freely opened. Left ventricle, two wounds; entrance wound near apex, exit wound near base. Both wounds closed with catgut sutures. Drainage of pericardium and pleura. Recovery.

The patient enjoyed good health for about two years, when he died of typhoid fever. The autopsy findings presented by Launay were as follows: There was almost complete adherence of the pericardium. Two soft depressions were present on the left ventricle; the anterior, where the bullet entered, was situated near the left margin 4 cm. from the apex; the posterior, was below the auriculoventricular groove near the left margin.

After opening the left ventricle there was visible on the anterior wall a white cicatricial zone on a level with the insertion of the anterior mitral pillar.

On the posterior wall of the left ventricle near the interventricular septum there was a cicatrix 2.5 cm. long. Its general form was oval, the lower extremity being larger. At that place the projections of the columnæ carnea were modified and the cicatrix slightly depressed.

Launay stated that no weak points could be recognized in the cicatrix, and that the obliquity of the parietal wounds explained the fact that in the operation hemorrhage stopped during systole.

Riche: Operation 1902. Female, aged thirty years. Stab wound in the fourth left space, parasternal line. Operation two hours after injury. Flap of third and fourth ribs, hinge external. Pleura freely opened. Wound 5 mm. in right ventricle, sutured, no drainage, no complications.

The patient was a delicate woman who did little work prior to the operation. She had a child in December, 1903, and another in July, 1905. Riche examined her on February 4, 1907, five years after operation. She had a pseudarthrosis of two costal cartilages. The heart was a little more vertical than normal. When the patient was made to lie on the right side and on the left side the heart became less displaced than normal, suggesting that there were some adhesions between the surfaces of the pericardium. The apex beat was near the sternum, in contact with the seventh cartilage. No abnormal sounds; function normal. The patient was as strong as before her attempted suicide. (Personal communication.)

Manteuffel (1903): Female, aged twenty-one years. Gunshot wound, fourth interspace. Operation about nine hours after the injury. Longitudinal incision at left sternal margin; resection of fourth, fifth, sixth, and seventh costal cartilages; removal of a strip of sternum 2 cm. in width. Entrance orifice, 5 cm. from apex, in right ventricle. Silk suture. Bullet in posterior wall of right ventricle; extraction, suture. Pericardium was closed with four sutures. No drainage of pericardium; pleura drained. Serous pericarditis followed; aspiration; the patient finally made a good recovery.

Patient was married in 1906; has two children. She was presented in 1905 before the Surgical Congress in St. Petersburg.

Was seen in 1914, eleven years after operation. Cicatrix slightly retracted; participates in pulsation. Limits of cardiac dulness and heart sounds normal. No functional disturbance of any kind.

In roentgenograph, the shadow on the right side projects beyond the sternal margin, and the angle at the left auricle is obliterated. At the base of the heart are seen peculiar feather-like shadows, which are perhaps to be interpreted as adhesions. The position of the heart is somewhat more horizontal than normal. (Personal communication.)

Borchardt: Operation, 1904. Male, aged twelve years. Impaled on picket fence. Hemopneumothorax. Two and a half hours between receipt of wound and operation. Incision from sternum to axilla; resection of sixth cartilage and rib. Left ventricle presented a wound 1.5 cm. long on posterior wall. Four silk sutures. Drainage of pericardium and pleura. Recovery.

The patient was last seen in 1911, seven years after operation. He was then in excellent health and capable of any work. (Personal communication.)

Sultan: Operation, 1907. Male, aged thirty-eight years. Pistol-shot wound in fifth left space just inside nipple line. Thirty hours between receipt of wound and operation. Flap of fourth and fifth left cartilages and part of sternum; hinge mesial. Pleura not opened. Hemopericardium, 200 c.c. Non-penetrating wound in posterior surface of left ventricle, 1.5 cm. long. Three silk sutures. No complications. Recovery.

The patient was last heard from in 1912, five years after operation. His health was excellent, and he was able to do his work as carpenter, which necessitated extreme exertion and heavy labor. The last examination was in 1910, three years after operation, when no deviations from the normal could be demonstrated. (Personal communication.)

Blake: Operation, December 13, 1907. Male, aged twenty-four years; colored. Stab wound through fourth left cartilage, 1 cm. within nipple line. Two and a half hours between receipt of wound and operation. Flap of third, fourth, and fifth cartilages; hinge internal. Pleura freely opened. Left pleura contained two pints of blood; pericardium about two ounces. Wound in right ventricle. Three interrupted silk sutures; one superimposed mattress suture. No drainage of pericardium or pleura. Gauze drain in stab wound. Double pneumonia; left empyema, drained on twenty-sixth day after operation. Wound infection. Recovery.

The patient was seen for the last time in March, 1907, when he was in good condition, heart action regular; pericardial friction sound. (Personal communication.)

Peck: Operation, 1908. Female, colored, aged twenty-three years, stab wound through third left cartilage at the border of the sternum. Flap of third, fourth, and fifth ribs; hinge external. Resection of part of the sternum. Pleura not opened. A wound, 1 cm., was found in right auricle. Four chromicized catgut sutures inserted. No drainage of pericardium. Recovery.

Patient died in the City Hospital of pulmonary tuberculosis. Autopsy showed extensive pulmonary miliary tuberculosis. Pericardium greatly thickened, with tubercles in fibrous coat; complete obliteration of pericardial sac, visceral and parietal layers being adherent throughout. Site of heart wound could not be identified; heart walls somewhat thinned, as commonly seen in adhesive pericarditis, otherwise normal. It was thought that the adhesive process was due to tuberculous pericarditis rather than to the effects of the trauma and operation. (Personal communication.)

Proust: Operation, 1910. Male, aged thirteen years. Gunshot wound mesial to the left nipple; fifth costal cartilage fractured by bullet. Time between injury and operation six hours. Exposure by osteoplastic flap following division of fourth to sixth cartilages near sternum. Pleura opened. Tangential wound of left ventricle near apex. Four deep sutures covered by superficial sutures.

Small rubber drainage tube into pericardium. Suture of the pericardium with interrupted catgut. High temperature and signs of pericardial effusion in second week. The patient also had some difficulty in swallowing. Little discharge; the drainage tube was removed and a large amount of bloody fluid escaped; improvement; temperature normal in less than forty-eight hours. Patient discharged well one month after operation.

Subsequent report of case from paper read before American Surgical Association, 1914.

Immediately after his discharge from the hospital the patient was engaged as messenger boy. He followed this occupation for three years and did not experience any trouble except at first, when he noticed some shortness of breath after hurrying up stairs. For the last year he has been employed as bookkeeper and complains of no trouble.

Auscultation and the electrocardiogram showed that the action of the heart was almost normal. The apex seemed a little too near the sternum and the electrocardiogram showed a double bracket at the time of the ventricular contraction. Radioscopic examination showed very slight modifications:

At the union of the external two-thirds and the internal third of the left border is seen a permanent notch, which seems to be a fixed point, and does not participate in the beating of the left border, as if at this level there were something restraining this margin. Moreover, below this notch is seen on the left ventricle itself a circular zone three-fourths of an inch in diameter, which is relatively clear in contrast to the deep color of the remainder of the ventricle. Proust explains the notch as due to adhesions and the clear zone as an abnormally thin condition of the myocardium following a scar.

A Roentgen-ray examination following the ingestion of bismuth showed a diminution in the diameter of the esophagus from the site of the large vessels to the diaphragm.

F. Hesse (1909): Stab wound, 1 cm. in length, in third left intercostal space, four fingers' breadth from sternum. Male, aged thirty-five years. Time between injury and operation nearly three hours. Wound in left auricle 0.75 cm. long. Resection of ribs and cartilages, also a strip of sternum. Pleura opened. Three silk sutures. Large rubber drainage tube into pericardium. Two drainage tubes into pleural cavity in scapular line by resection of rib. Discharge from pleural cavity profuse, from pericardial cavity slight, so that drain was removed on fifth day. Pleural drain left for a month. Recovery.

Examination of patient on discharge showed a small granulating area, otherwise a normal scar. Lower border of left lung is one to one and a half fingers' breadth higher than the right. Lungs otherwise normal.

Cardiac boundaries normal. Sounds loud and clear. No pericardial friction sounds. Pulse regular and equal but slightly accelerated. Patient feels a sense of oppression in region of heart on slight exertion.

Examination of patient two years after discharge: slight systolic retraction in fifth interspace mesial to midclavicular line. Heart sounds clear but diminished in intensity. Pulse 80 to 90. After exercise slight arrhythmia.

F. Hesse (1909): Stab wound 1 cm. long in third left intercostal space near sternum. Male, aged twenty-four years. Pronounced heart tamponade. Time between injury and operation, two and a half hours. Left auricle, 0.75 cm. Flap with external pedicle of third and fourth cartilages and part of ribs; resection of half of adjacent sternum; section of fifth rib. Pleura opened. Three silk sutures. No drainage. Recovery.

Examination of patient two years after discharge: Patient says his hands frequently become blue and cold; and that he sometimes feels a sharp pain in the chest especially after exertion. The precordium is markedly flattened and there is a distinct systolic retraction in the fifth interspace for a distance of 4 cm. inside of the midclavicular line. Right border extends to midsternal line at level of third rib. Heart sounds are slightly roughened at the apex; at the base they are clear but diminished in intensity. Pulse is full, regular, and equal.

F. Hesse (1909): Stab wound, 2.5 cm. long, under left nipple, in fourth intercostal space. Male, aged seventeen years. Hemopneumothorax. Time between injury and operation three hours. Wound in left ventricle a little below the atrioventricular boundary. Resection of fourth rib from nipple to sternum; pleura opened. Five silk sutures. Removal of clots from pleural cavity. No drainage. Pleurisy and pneumonia. Entire wound opened and healed gradually. Recovery.

Examination of patient in April, 1911, two years after operation: Patient has resumed his work as porter and says that he experiences no discomfort either during rest or exertion. The sternal end of the scar is markedly depressed, enough to admit two fingers into the depression. Over this region the skin is red and tender and united with the pericardium. Heart impulses are readily felt in this area. Cardiac boundaries extend from midsternal line to 1 cm. outside of left nipple, which has moved 1 cm. inward and 1 cm. upward. Heart sounds are regular.

E. Hesse (1905): Stab wound, 3 cm. long, parasternal line, fifth intercostal space. Male, aged nineteen years. Heart tamponade. Time between injury and operation one hour. Penetrating wound of right ventricle. Incision along left sternal margin and fifth rib; resection of sternal segments of fourth, fifth, sixth, and seventh ribs. Three sutures. Drainage of pericardium. Drainage of pleura through wound. Change of dressings on fifth day; tampons soaked. Recovery.

Examination of patient on discharge from the hospital: Wound healed. Percussion of heart shows a lengthening of horizontal measurements; vertical measurements normal. Heart sounds are clear and distinct. Pulse is 90. Rhythm normal. Blood-pressure 80. Lungs normal. No dyspnea on exercise.

Five years after the operation the patient wrote saying that he was perfectly well and doing his regular work.

E. Hesse (1908): Stab wound, 2 cm. long, between fourth and fifth costal cartilages, one and one-half fingers' breadth to left of sternum. Male, aged twenty-one years. Stab wound of abdomen, viscera uninjured. Time between injury and operation an hour and a half. Wound in right ventricle, 1 cm. Skin-muscle flap, resection of cartilages of fifth and sixth ribs. Two deep sutures. Pericardium and pleura closed. No drainage. Pneumonia on fifth day. Empyema, thoracotomy on eighth day. Obstinate septic diarrhea on twelfth day. Dry pericarditis on fifteenth day. Improvement began fifth week. Discharged, in good condition, in eleven weeks.

Examination on discharge from hospital: Patient in good condition. No dyspnea or dizziness. Pulse strong and accelerated. Heart sounds clear.

Two years and seven months after the operation patient wrote that he was well and working.

E. Hesse (1909): Gunshot wound between fourth and fifth ribs, two fingers' breadth to right of nipple. Exit orifice about four fingers breadth below left scapular angle. Male, aged seventeen years. Time between injury and operation an hour and a half. Resection of fourth and fifth ribs with cartilages, about 7 cm. Wound of left lung. Wound of left ventricle. Three sutures in heart. Suture of pulmonary wound. No drainage. Empyema (left); thoracotomy. Pericarditis sicca. Dry pleurisy on right side. Recovery.

Examination on discharge from hospital: Wound healed. Cardiac area and sounds normal. In the apex of the lung there were some signs of beginning tuberculosis.

Examination in October, 1910: There is a sinking in of the chest between the sternum and the left mammary line over the third, fourth, and fifth ribs; systolic retraction over this area, especially over the fifth rib. Heart and lungs normal except for a diminished vesicular murmur and impaired resonance in left lower lobe of lung. Cardiac border extends to two fingers' breadth mesial to left mammary line and on the right does not extend beyond right sternal border. Heart sounds are clear. Aortic sounds are louder than the pulmonic. Pulse is accelerated (112) but rhythmic. Liver not palpable. No edema. An orthodiagram shows heart boundaries distinct. Diaphragm is movable on right side but not on left side where it shows adhesions. The blood-pressure was 110 systolic, 70 diastolic.

The patient says that while resting he feels perfectly well, but that on suddenly changing his position or during emotional periods he suffers from palpitation of the heart.

In April, 1911 (two years after operation), patient writes that he is well and has no untoward symptoms.

E. Hesse (1909): Stab wound, 2 cm. above and to right of left nipple. Male, aged twenty-eight years. Injury of branches of coronary artery. Time between injury and operation four hours. Wound of left ventricle, anterior surface near apex, 1 cm. Resection of fourth rib. Two sutures. Suture of pericardium and pleura. No drainage. Recovery.

Examination of patient one and a half years after operation: There is a slight systolic retraction of the scar. Heart boundaries and sounds good. The diaphragm is freely movable on right side but is adherent on the left. Blood-pressure is normal. Pulse 90 and good quality. Orthodiagram: Heart boundaries distinct and normal. On right side the diaphragm is 6 cm. deeper than on left. Shadows show adhesions on left side. The patient is in good condition and does not complain of any symptoms after hard work.

E. Hesse (1910): Stab wound, about 1.5 cm. long, between fifth and sixth ribs, left side, between nipple and anterior axillary line. Male, aged twenty-seven years. Time between injury and operation one and three-quarter hours. Wound of left ventricle, 2 cm. long, about 5 cm. from cardiac apex. Resection of fourth and fifth ribs, to extent of 6 to 7 cm. from sternum. Three sutures. Suture of pericardium and pleura. No drainage. Left-sided pneumonia on fourteenth day.

Examination of patient twenty-five days after operation showed an absence of pericardial friction sounds and normal cardiac sounds.

Examination eight months after operation: Scar smooth; presystolic but no systolic retraction of the scar. Cardiac outline. Above: to the third rib; left: just mesial to mammary line; right: not beyond right sternal border. Heart sounds are clear. Second pulmonic sound is louder than aortic. Pulse 90 and of good quality. Blood-pressure 115 systolic; 75 diastolic. No venous pulse present. An orthodiagram shows sharp outline of heart except at apex, where there probably are some adhesions. No cardiac enlargement present. No dyspnea. Patient can exercise without disturbance.

E. Hesse (1903): Stab wound, 1.5 cm. long, in second intercostal space, about 2.5 fingers breadth from left sternal margin. Female, aged twenty-five years. Time between injury and operation three hours. Wound of left ventricle, 0.5 cm. Skin-muscle flap, resection of third and fourth cartilages. One suture. Pericardium and pleura sutured. No drainage. Recovery.

Surgeon.	Age.	Sex	Cause of wound.	Site of superficial wound.	Time between accident and operation.	Site of heart wound.	Postoperative complications.	Material of suture used in heart wound.	Drainage of pleura.	Drainage of [into] pericardium.	Time of last examination after operation.	Condition at time of last examination.
Blake	24	M	Stab	4th space, 1 cm. inside of nipple line	2¼ hrs.	Right ventricle	Double pneumonia and empyemia and wound infection	Silk	No	Secondary	March, 1907, 3 months	Pericardial friction sounds present. Patient in good health.
Borchardt	12	M.	Fell on picket fence	5th space midmammary line	2½ hrs.	Left ventricle, along posterior border	Pericarditis, bilateral pleurisy and bronchopneumonia	Silk	Yes	Yes	7 years	Patient in excellent health and capable of any work.
Launay	26	M	Gunshot	Left nipple	4 hrs.	Left ventricle, 2 wounds; entrance near apex, exit near base	None	Catgut	Yes	Yes	2 years; patient died of typhoid; autopsy	Autopsy 2 years later; death due to typhoid; marked pericardial adhesions; no weak points in cicatrix; good health for two years.
Manteuffel	21	F.	Gunshot	4th left interspace	9 hrs.	Entrance wound; right ventricle 6 cm. from apex; bullet in posterior wall	Serous pericarditis (aspirated)	Silk	Yes	No	11 years	Slight retraction of cicatrix; few pericardial adhesions at base of heart; health perfect.
Parlavecchio	20	M.	Stab	5th left interspace	8 hrs.	Left ventricle near apex	None	Silk	No	No	15 years	Examination negative except for systolic retraction at cicatrix.
Peck	23	F.	Stab	3d left cartilage at border of sternum	45 min.	Right auricle	Slight pleurisy	Chromic gut	No	No	....	Autopsy; death due to pulmonary tuberculosis; extensive pulmonary miliary tuberculosis; pericardal sac obliterated; many tubercles in pericardium; site of heart wound could not be identified.
Pool	24	M.	Stab	4th space close to border of 5th rib just inside nipple	50 min.	Left ventricle at left margin of heart	None	Vaselined silk	No	No	3 years	Good health; capable of doing hard work.
Proust	13	M.	Gunshot	5th costal cartilage mesial to left nipple	6 hrs.	Left ventricle near apex	High temperature and signs of pericarditis and effusion in 2d week	Catgut	No	Yes	4 years	Pericardial adhesions; general condition good.
Riche	30	F.	Stab	4th left space parasternal line	2 hrs.	Right ventricle	Dyspnea and attack of suffocation	Catgut	No	No	5 years	Pseudo-arthrosis of two costal cartilages. Adhesions of pericardium; general condition as good as before operation.

Sultan	38	M.	Gunshot	5th left space just inside nipple line	30 hrs.	Non-penetrating wound posterior surface left ventricle	None	Silk	No	No	3 years	Patient in good health and capable of doing heavy work.
F. Hesse	35	M.	Stab	3d left interspace 4 fingers' breadth from sternum	3 hrs.	Left auricle	Profuse discharge from pleural cavity, slight from pericardium	Silk	Yes	Yes	2 years	Systolic retraction in 5th interspace; mesial to mid-clavicular line; slight arrhythmia after exercise; health good.
F. Hesse	24	M.	Stab	3d left space near sternum	2½ hrs.	Left auricle	....	Silk	No	No	2 years	Systolic retraction in 5th interspace 4 cm. inside mid-clavicular line; heart sounds roughened at apex.
F. Hesse	17	M.	Stab	4th space under left nipple	3 hrs.	Left auricle, little below atrioventricle boundary	Pleurisy and pneumonia	Silk	No	No	2 years	Marked depression of scar; patient in good condition and capable of doing heavy work.
E. Hesse	19	M.	Stab	5th space parasternal line	1 hr.	Right ventricle	....	.....	Yes	Yes	5 years	Patient in perfect health; examination negative; perfect health; does hard work
E. Hesse	21	M.	Stab	Between 4th and 5th cartilage, 1¼ in. to right of nipple	1½ hrs.	Right ventricle	Pneumonia, empyemia, septic diarrhea	.....	No	No	2 yrs. 7 mos.	Patient in perfect health and doing his regular work.
E. Hesse	17	M.	Gunshot	Between 4th and 5th ribs, 1½ in. to right of nipple	1½ hrs.	Left ventricle	Empyemia (left); drypleurisy (right)	.....	No	No	1 year	Systolic retraction over sunken area between sternum and left mammary line, 3d, 4th and 5th ribs; well and experiences no discomfort.
E. Hesse	28	M.	Stab	2 cm. above and to right of left nipple	4 hrs.	Left ventricle; anterior surface near apex; injury to branches of coronary artery	....	.....	No	No	1½ years	Systolic retraction of scar; adhesions on left side; good condition and does not complain of any distress afterhard work.
E. Hesse	27	M.	Stab	Between 5th and 6th ribs; between left nipple and anterior axillary line	1¾ hrs.	Left ventricles 5 cm. from apex	Pneumonia	.....	No	No	8 months	Presystolic retraction of scar; can exercise without disturbance.
E. Hesse	25	F.	Stab	2d space, 1½ in. from sternal margin	3 hrs.	Left ventricle	....	.....	No	No	7 years	Slight enlargement of heart toward the right; heart sounds distant, clear, and rhythmic; no subjective symptoms.
Grisogono	18	M.	Stab	3d space, 2¼ in. from mammary line	¾ hr.	Left auricle	Pneumothorax	Silk	Yes	No	1 year	Patient practically normal.
Foederl	25	M.	2 stab wounds	One above 4th rib; other below 4th rib	..	Left ventricle	....	.....	No	Yes	7 years	Patient well.

SUMMARY.

Number of cases		21
Age	Between 20 and 30 years	13
	Between 12 and 20 years	6
	Between 30 and 38 years	2
Sex	Males	17
	Females	4
Cause of wound	Stab	15
	Gunshot	5
	Other cause	1
Site of superficial wound	Fourth to fifth left space	15
	Above fourth space	6
Time between accident and operation	One-half to one hour	4
	One to two hours	4
	Two to three hours	6
	Three to four hours	2
	More than four hours	4
Site of heart wound	Right auricle	1
	Left auricle	4
	Right ventricle	5
	Left ventricle	11
Post-operative complications	Pneumonia	5
	Empyema	3
	Pericarditis (serous)	4
	Pleurisy (non-purulent)	5
	Pneumothorax	1
	Marked dyspnea	1
	None	9
Material used in suture of heart wound	Silk	10
	Catgut	3
	Chromic	1
	Not mentioned	7
Drainage of pleura	Yes	6
	No	15
Drainage of pericardium	Yes	6
	No	15

Examination three weeks after operation: Heart normal. Pulse shows great oscillations, due probably to an increased irritability of the cardiac nerves.

Examination ten and a half months after operation: There is a systolic retraction of the scar. Heart sounds are regular, dull but clear. Pulse is dicrotic (96) and regular. No subjective symptoms present.

Examination seven years after operation: Patient was admitted for pneumonia. No cardiac symptoms present. There was a slight enlargement of the heart towards the right; the upper boundary extended to lower border of third rib; left border extended to one finger's breadth medial to nipple line. Heart sounds distinct and clear. Pulse rhythmic and good quality. Slight systolic retraction of scar present.

Foederl (1903): Two stab wounds, one above and the other below the fourth rib. Male, aged twenty-five years. Symptoms of progressive hemopericardium. Pleura intact. Wound of left ventricle, 1 cm. Flap of third and fourth cartilages, without injury to the pleura. Two sutures. Drainage of pericardium with gauze. Protracted course; thoracotomy. Recovery. Patient well at time of report, seven years after operation.

Grisogono: Stab wound in third intercostal space, three fingers' breadth from mammary line, 1.5 cm. in length. Male, aged eighteen years. Pneumothorax; hemopericardium without signs. Time between injury and operation forty-five minutes. Wound 1.5 cm. long, left auricle. Triangular skin-muscle flap. Resection of third and fourth cartilages for 7 cm. from sternum and 5 cm. of second. Four silk sutures. Pleural cavity drained with gauze through lower angle of wound. Pericardium, no drainage. Pneumothorax. Slow recovery; discharged well two and a half months after operation. A year later practically normal.

The table on pages 348 and 349 presents for comparison the important features of these cases. Few deductions can be drawn from these statistics, since they are compounded from an extremely limited number of cases. However, it is striking that in all cases of which we have records a long period after operation, the general condition of the patients was apparently normal. The patients were able to perform arduous work without discomfort, and for the most part without experiencing any subjective symptoms. It is noteworthy that in these cases suppurative pericarditis did not occur as a postoperative complication.

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REMOVAL BY CAFFEIN OF SOME DIGITALIS ARRHYTHMIAS: ILLUSTRATED BY TRACINGS.

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When digitalis is administered in cases of heart failure in which the auricles are fibrillating the gross irregularity of the ventricle observed in this condition is not materially lessened, although, as is well known, the rate of the heart beat is greatly slowed and the subjective symptoms are often magically ameliorated.

In cases of heart failure in which the rhythm is normal, digitalis slows the pulse only moderately, and what is of considerable interest, tends often to induce irregularities of several different kinds, chief of which are premature contraction and heart block. I have observed in several instances of marked heart failure after prolonged use of digitalis the appearance of dicrotism, and when this dicrotism is unaccompanied by pulsus alternans it is removed by caffein.

Premature contractions produced by digitalis are fairly common, and are usually of ventricular origin. Partial heart block following digitalis is also very common. In some cases of digitalis block the *As–Vs* interval is found widened previously to or concomitantly with the block, while in other cases this phenomenon is not observed. Partial heart block and premature contractions following digitalis are often associated.

Digitalis heart block has been attributed by some to reduction of conductivity of the auriculoventricular bundle, by others to increase of vagus inhibition. In favor of the latter hypothesis is the fact that the block can be partly removed by atropin; in favor of the former view is the fact that in auricular fibrillation digitalis slows the heart chiefly by depressing the conductivity of the bundle. As a matter of fact, both factors may be involved, and in the present state of our knowledge we cannot define absolutely their relative values.

Digitalis is known to slow the heart rate while caffein accelerates it. If the slowing by digitalis is partly produced by lowering the irritability of the conduction system the effect of caffein in accelerating the rate is partly due to an opposite effect. Caffein tends to raise the irritability of the conducting system. It should therefore theoretically neutralize or possibly overcome the effects of digitalis upon the heart. My investigations have tended to show that the cardiac effects of digitalis, particularly in respect to interference with conduction, are quickly overcome by caffein. For some time past in the hospital wards I have observed the effects of caffein in cases which showed digitalis arrhythmias, and the following seven cases briefly reported are selected from a considerable number to show that the theoretical considerations above mentioned are borne out by the facts.

Digitalis irregularities will usually cease spontaneously if the drug is stopped, but sometimes instances arise in which, unfortunately, the drug has been prolonged in its administration until the toxic effects upon the conducting system are only too manifest, and in these the administration of caffein will do good.

The first two cases show pulsus bigeminus, due to extreme dicrotism under circumstances of great enfeeblement of contractility. The second case shows marked pulsus alternans. This case died suddenly at the time when the experiment of administering caffein was about to be tried, and the tracing is shown because it is similar to Case I with respect to dicrotism; but there is one important difference, and that is that in Case II pulsus alternans is present, which is, under all circumstances, of extremely grave augury. In Case I the arrhythmia disappeared as soon as caffein was given.

Two cases are given in which block arose as a result of digitalis administration and one of spontaneous block. In all, the phenomenon of block was readily removed by caffein, as the tracings show.

I have seen block removed by caffein at times even while digitalis was being taken. It would appear that partial heart block or premature contraction is the rule rather than the exception when digitalis is kept up even in moderate doses for a long period of time in cases of heart failure with normal rhythm, and it is my experience that these disturbances of rhythm can be quickly removed by caffein.

One case of auricular fibrillation is given to show that caffein has no effect upon the irregularity itself any more than has digitalis, but nevertheless the rate increases under caffein even during digitalis administration, which tends to show, I believe, that the conductivity of the bundle of His lowered by digitalis is increased by caffein.

Case I.—*Dicrotic pulsus bigeminus occurring in a case of heart failure; normal rhythm; prolonged digitalis administration; recovery.*

C. B. entered hospital November 12. From date of admission, November 12, to January 12, a period of two months, the patient ingested 7 grams of powdered digitalis and 3 ounces of the tincture. On January 7 a tracing was taken (*a b*) which showed marked dicrotism.

January 13 digitalis was stopped and caffein sodium citrate, grs. iij, t. i. d, substituted.

January 18 a tracing of the radial pulse showed an almost complete disappearance of dicrotism (*v c*). Concomitantly with this there was an improvement in the patient's condition.

January 31 strips of radial pulse tracings taken on this day showed a complete absence of dicrotism (*v d e*). The pulse was regular and beating 72 to 80 per minute. Patient left the hospital apparently cured.

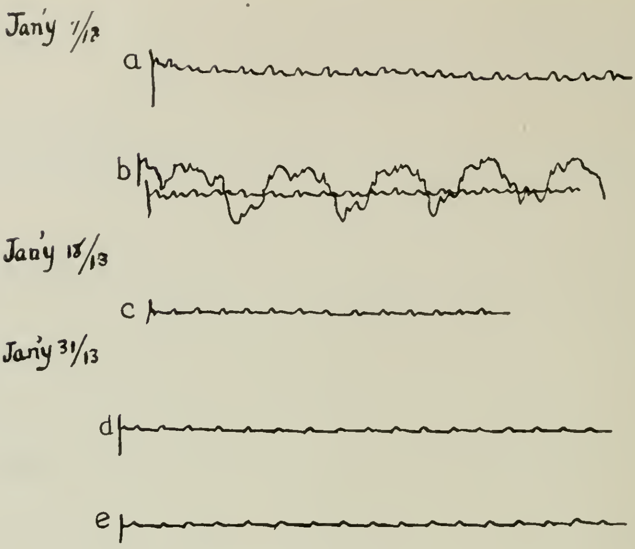


FIG. 1.—Case I, C. B.

CASE II.—*Dicrotic pulsus bigeminus with pulsus alternans; extreme heart failure; rapid but normal rhythm; prolonged digitalis administration; sudden death.*

J. H. entered hospital January 13. Between admission to hospital and February 5 he received 49 ounces of tincture of digitalis. On February 6 he was given powdered digitalis, and up to February 22 he took $8\frac{1}{2}$ grams.

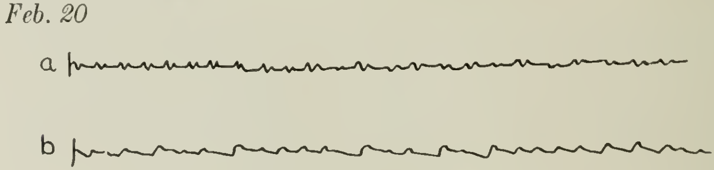


FIG. 2.—Case II, J. H.

On February 20 radial pulse tracings were taken. It was impossible to obtain jugular tracings on account of extreme respiratory distress. The radial pulse was dicrotic and showed pulsus alternans (*v a b*). He died suddenly during the night of February 22.

CASE III.—*Heart failure with normal rhythm; partial heart block and pulsus bigeminus removed by caffein; exitus.*

H. S. entered hospital September 6. September 27 a pulse tracing showed feeble rapid pulsations but normal rhythm. Jugular tracing shows absence of *v* waves (*v a b*). From the date of admission, September 6, until January 19, a period of 135 days, the patient took in all 10 grains of strychnin, 540 grains of caffein citrate, and 33 ounces (one quart) of infusion of digitalis. On

January 20 a tracing of the radial pulse showed partial heart block with occasional slight tendency to dicrotism and bigeminism (*v c d e*). Digitalis was stopped on January 21 and caffein sodium benzoate grs. iij, opium gr. ss, and calomel gr. ss, t. i. d., substituted.

January 27 the polygraphic record showed complete disappearance of the block.

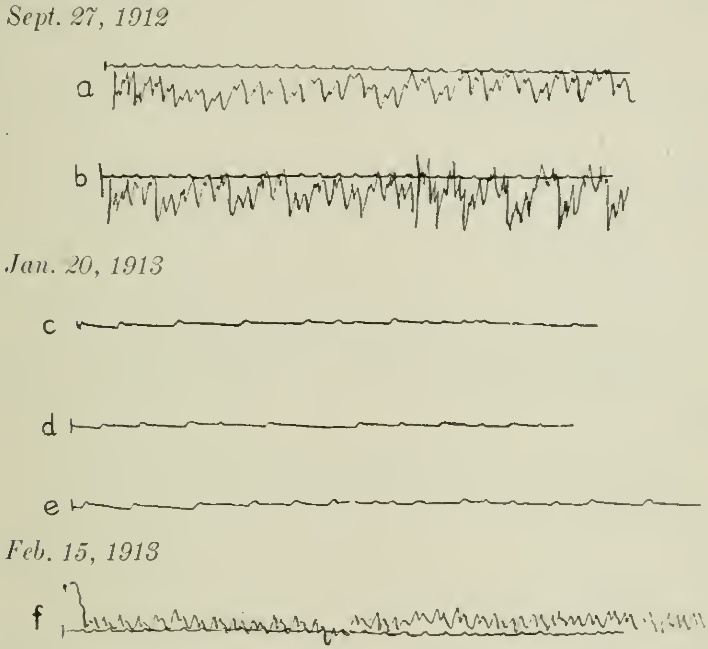


Fig. 3.—Case III, H. S.

A tracing taken on February 15 showed no block. The radial pulse was extremely small and showed a trace of dicrotism (*v f*). For five days preceding February 15 digitalis had been again given, ♏xv, t. i. d. The patient died soon afterward and autopsy showed a much dilated heart, with extremely thin, flabby musculature and wide, patulous mitral orifice.

Case IV.—*Auricular fibrillation; digitalis slowed the pulse but did not abolish the irregularity; the rhythm was unaffected by caffein.*

This case, which was entirely similar to others observed in this regard, demonstrates that caffein is apparently without effect upon the rhythm of auricular fibrillation.

Kate G., aged sixty years, entered hospital on January 21. A tracing taken on January 23 showed the auricles were fibrillating. The pulse was rapid and extremely irregular, and there was a total absence of *a* wave in the jugular tracing (*v a*). The patient was put on tr. digitalis, ♏x, t. i. d., for a week.

January 27. A strip of radial tracing showed no change (*v b*).

January 30. Tracings taken and conditions found unchanged (*v c*).

February 6. Tracing taken and the conditions the same (*v d*). Caffein sodium citrate began, gr. iij, t. i. d., on February 7 and continued until February 19. No change was noted.

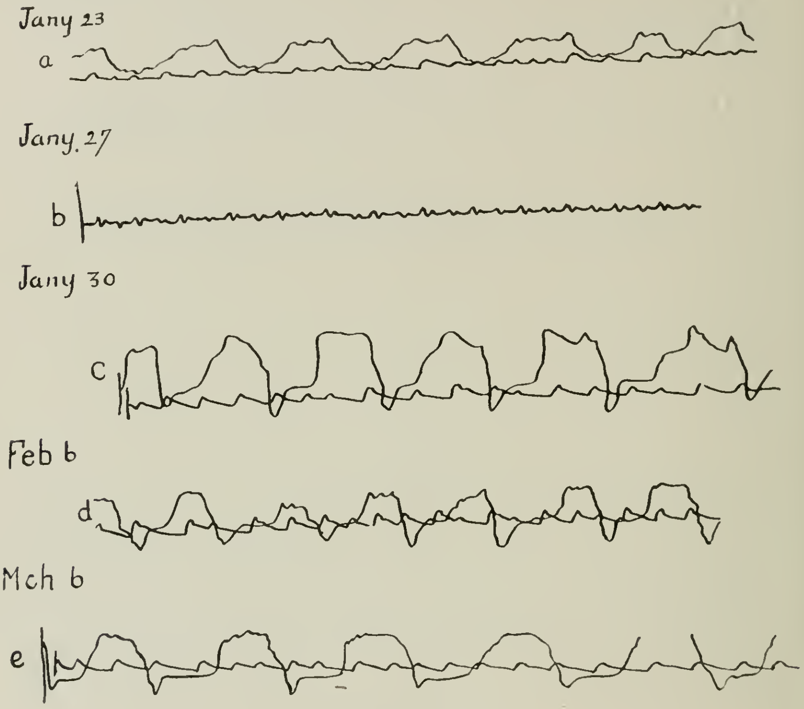


Fig. 4.—Case IV, K. G.

March 6. Tracing taken. Result unchanged (*v e*). Patient was put back upon digitalis February 19, one dose per day of 10 minims, which was found sufficient to keep the heart slowed and ameliorate the subjective symptoms. Patient was discharged about the middle of March.

Case V.—*Heart failure accompanying mitral insufficiency with a secondary tricuspid regurgitation; normal rhythm; premature contractions and partial heart block produced by digitalis; removal by caffein.*

J. J. entered hospital January 25. Tracings were taken January 27 and showed practically normal rhythm (*v a*). The patient was put on tincture of digitalis, ♏xv, t. i. d. Nine days later, February 6, tracings were taken, all of which showed premature contractions and partial block.

February 6. Digitalis was discontinued and caffein sodium citrate, grs. iij, t. i. d., substituted (*v b c d*).

February 10. Strips of radial pulse tracing were taken and showed complete disappearance of the arrhythmia (*v e f*).

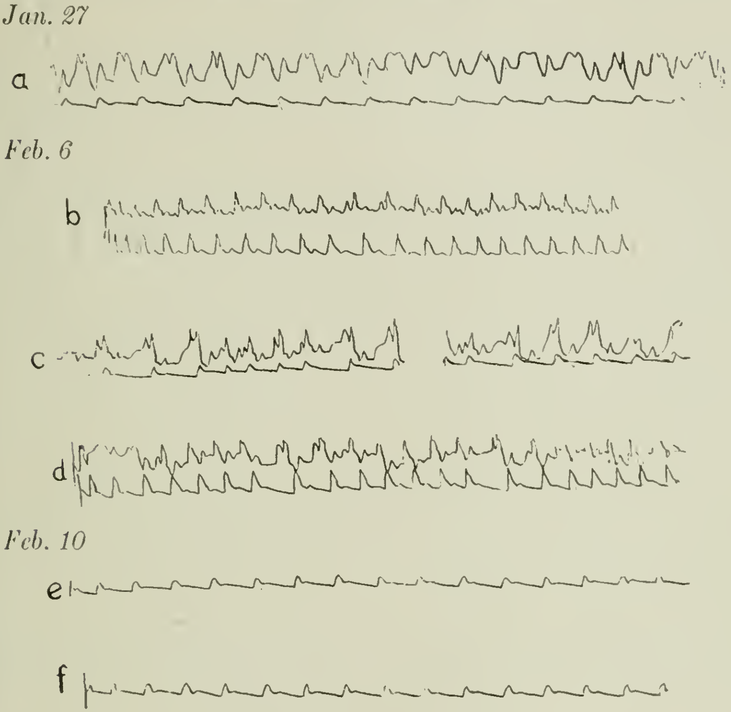


FIG. 5.—Case V, J. J.

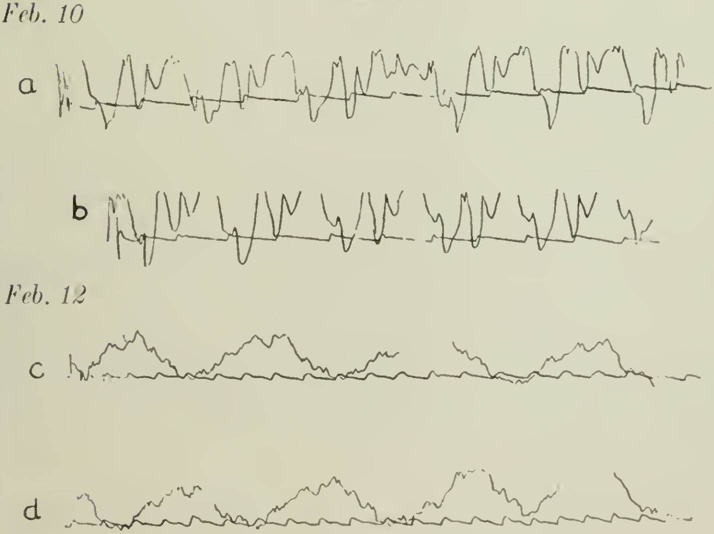


FIG. 6.—Case VI, Mrs. D.

Case VI.—*Partial heart block of sino-auricular type produced by digitalis in a case of moderate heart failure in a pregnant woman; normal rhythm; removal of block by caffein.*

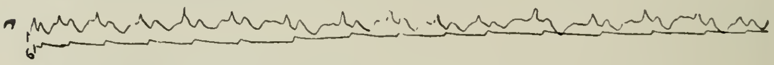
Mrs. D. entered hospital in March. She was near term and suffering from symptoms of heart failure accompanying mitral regurgitation. The cardiac rhythm was normal. The patient was given tincture of digitalis, ♏x, t. i. d., and kept upon it for for some time.

Tracings taken February 10 showed partial heart block (*v a b*). Digitalis was immediately stopped and caffein sodium citrate, grs. iij, t. i. d., substituted. Two days later tracings showed complete absence of the arrhythmia (*v c d*).

Case VII.—*Spontaneous heart block with pulse rate of about 46 to 48; caffein diminished the block and raised the pulse frequency to 74 to 76.*

Admitted to hospital March 14. Patient was an elderly man. Tracings taken March 18 showed 2 to 1 heart block (*v a*). He was given caffein sodium citrate, gr. v, t. i. d. A tracing taken five days later, March 23, showed almost complete disappearance of the block. Pulse increased to 74 (*v b*).

March 18, radial pulse 46



March 23, radial pulse 74

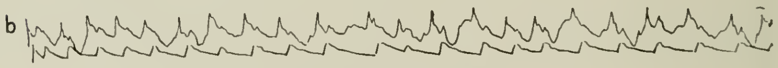


Fig. 7.—Case VII, G. W. T.

Case VIII.—Spontaneous heart block.

Conclusion. All the irregularities of the heart beat which are brought about by digitalis tend to be removed by caffein. Although in many cases digitalis arrhythmia will spontaneously disappear when the drug is stopped, instances arise, unfortunately too common, in which after prolonged digitalis administration the conductive system is so depressed that serious results may arise. Under these circumstances the administration of caffein will be of service and therefore strongly indicated. The action appears to be due to the increase in irritability of the conduction system produced by the caffein, which antagonizes and finally overcomes the depressing effects which digitalis exerts upon the auriculoventricular bundle.

BRAIN SYPHILIS.

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In considering a disease as essentially polymorphic as syphilis of the central nervous system, it is not surprising that apart from certain well-defined clinical and microscopic pictures there should be observed conditions not so clearly defined, forming through the coexistence of different manifestations of these would-be entities, cases that cannot clinically or pathologically be diagnosed according to hard and fast lines.

Duchenne,[1] in 1859, observed that "some (ataxic) patient had suffered from syphilis." A few years later Schultze pointed out the importance of the association of syphilis with ataxia, and in 1876 Fournier insisted on the frequency of a previous history of syphilis in tabetics. Raymond[2] stated, "It is not proved, but it is extremely probable, that syphilis has a part direct or indirect in the causation of tabes dorsalis when this disease shows itself in syphilitics." Vulpian, Erb, and Gowers each subsequently contributed extensively in support of the view of Fournier. General paralysis had likewise been associated with syphilis, but we do not find the connection as definitely stated except by Fournier,[3] who in his classification of syphilis of the central nervous system included tabes, general paralysis of the insane, special forms of epilepsy, and muscular dystrophies. Ford Robertson advanced the view that general paralysis was the result of a bacterial toxic infection from the respiratory and alimentary tracts, owing to the impairment of the resisting powers of the organism by syphilis, alcoholism, or excessive use of nitrogenous foods. Ferrier[4] stated, "We are dealing with merely different aspects of the same polymorphic disease." Mott maintained "that etiologically and pathogenetically there is one tabes which may begin in the brain (especially in certain regions), or in the spinal cord in certain regions, or in the peripheral nervous structures connected with the viscera, constituting, therefore, different types, any of which may be present or be associated with one or all of the others." Moebius and Shaffer made no less positive statements. Lang and Neisser were the first to ascribe the dependence of the tertiary lesion of syphilis to the activity of the virus. To Lang also is due the credit of having first noted the occurrence of meningeal involvement with general dissemination of the virus. Thus the concept of syphilitic disease of the central nervous system has, more especially since the discovery of modern microscopic and serological methods, gradually been enlarged, until today it includes not only possible syphilitic entities of the central nervous system, but also conditions simulating most every other known possible disease of that system.

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[1] Arch. gén. de méd., ser. V, 1859, 439.

[2] Le Progrès Médicale, 1892, 453.

[3] Gazette Médicale de Paris, 1876, No. 53.

[4] Lancet, 1906, 951.

Long before the discovery of the Spirocheta pallida by Schaudinn and their demonstration by Noguchi and Moore, Moebius and Erb advanced the theory of the possibility of a form of the syphilitic virus falling with special incidence on the spinal and cerebral centres and leading in due course to tabes or general paralysis to account for the different manifestations of the effects of syphilitic inoculation. Brosius related the history of seven glass-blowers infected in the mouth from the same source in 1891. After twelve years five came under his observation again. One was tabetic; a second had signs of general paresis; the third was a marked general paretic; the fourth had indications of tabo-paresis; the fifth was still in good health. Raymond reported a case of two brothers syphilized at the same time; one lead a fast life and indulged in sexual excess and later developed tabes; the other led an industrious life accompanied with many financial worries and later developed general paresis. Souques described a family in which the father was syphilitic and became a general paretic; the mother became a tabetic and two young daughters also showed signs of tabes. Morell-Lavallée described the case of one woman who infected five men, four of whom developed general paresis and the fifth syphilitic meningitis. Mott mentioned two men syphilized by the same nurse, and ten years later both developed general paralysis, while Marie and Bernard described two men who had acquired syphilis from the same source and who later developed tabes dorsalis.

Noguchi found some evidence for the possibility of considering a special strain in the fact that the organisms obtained from cases of general paresis had markedly long periods of incubation. As an explanation of this surely a possible attenuation or modification of the virus must be considered. From the present data and knowledge of the essential similarity of the microscopic findings there is strong evidence that the general or focal character of the lesions depends upon certain conditions. Where the vitality of any given part is lessened, as by impaired blood supply or by trauma, this part is more favorable for spirochetal development. In other instances it appears that the syphilitic process in attacking a certain definite region of the central nervous system has less tendency to become a general process, and does so almost to the exclusion of other parts. That the location of the virus is of variable intensity has been demonstrated by Levaditi, A. Marie, and Bankowski[5] who stated

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[5] Annales de l'Institute Pasteur, Juilliet, 1913.

"the abundance of parasites varies greatly from one case to the other; at times the treponema are exceedingly abundant, at times very rare. They are generally grouped in 'foyers,' more or less circumscribed, especially in the anterior regions of the cortex, but have also been seen in the bulb, cord, and spinal ganglia." It has long been considered that not only different individuals but even different races offer increased resistance to the Treponema pallidum, and it has been proved that even the tissues of the body show varying resistance, the heart showing little and frequently no response to the presence of the organism. Can not the absence of correlation between the severity of the early manifestation of syphilitic infection and the late ones, and also between the time of inoculation and the period of onset of the symptoms, be explained by individual resistance or possible immunization as well as by the theory of different strains of the virus? How is one to account for the simultaneous occurrence of combined involvement of different parts of the central nervous system and for the exacerbation of spirochetal involvement at the site of trauma? The former possibly on the theory of a mixed infection or strain, but certainly the latter on the evidence of lowered resistance of the part affected. Of common observation is the fact that many infected with syphilis who exhibit early symptoms that are so mild and frequently so slight that they may be unaware of them may develop severe disease of the central nervous system, whereas others with pronounced early manifestations may give no evidence of involvement of the central nervous system. The idea has been advanced that the virus having spent itself in early proliferation left an attenuated organism unable to affect severely the nervous tissues. Here again we may be dealing with an especially resistant nervous system, or the infected individual may have died of some incurrent infection before the breaking down of this resistance. Kern[6] stated that his findings of 85 per cent. of either the asthenic or emphysematous type of patients in his cases of tabes has convinced him that tabes should be designated "spinal syphilis with constitutional inferiority, predominately of the asthenic type." Mott[7] first observed that in spite of sexual promiscuity of many general paretics in the early stages of the disease he had never seen a primary sore in such an individual, and later Krafft-Ebing, as proof that the body is immunized by one infection, selected nine patients with general paralysis of the insane, and inoculated them by injecting the virus from a typical hard chancre; none of them developed syphilis, showing that they had become insusceptible to the disease.

The variability in time of onset of symptoms after inoculation may be of diagnostic importance in differentiating the types of syphilitic disease of the brain, but here again one is dealing with an unreliable factor. Blumel, Schaffer, and Nonne have reported cases of tabes occurring as early as one to one and a half years after infection. Frey observed tabetic symptoms in the third and fourth month after infection. Spiller has observed two cases of syphilis of the central nervous system while the rash was still on the body, one being a case of Brown-Séquard paralysis and the other a hemiplegia. Manifestations of syphilis of the brain have been quoted as occurring as early as four months after infection, and one case of general paresis has been described by Nonne as occurring as late as thirty years after infection.

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[6] Therap. Monat., Berlin, 1914.

[7] Proc. Roy. Soc. Med., 1909–10, vol. iii.

The symptomatic manifestations of syphilitic disease of the central nervous system are aside from clear-cut cases equally as relative and depend upon the localization of the syphilitic process and the susceptibility of the tissues. Disease of the optic nerve manifested by varying degrees of impaired vision and transitory or permanent amaurosis is observed in all syphilitic disease of the central nervous system. The frequency of loss of pupillary reaction to light with preservation of the reaction to accommodation observed by Argyll-Robertson in 1869 was first associated with tabes by Erb. Gowers,[8] in 1881, stated "That it may be taken as a practical rule that, apart from general paralysis of the insane, reflex iridoplegia always indicates either syphilis or tabes." Today the Argyll-Robertson pupil is considered the most common manifestation of parenchymatous syphilis, and it is found in cases of general paralysis and cerebral syphilis. That the Argyll-Robertson pupil is no longer absolutely diagnostic of syphilitic involvement of the nervous system is shown by the observation of Vincent,[9] who has reported a case of unilateral Argyll-Robertson pupil as the result of trauma; by that of Nonne and Wohlivell,[10] who reported its occurrence in alcoholism, and also that of Dejerine and Mirallee,[11] Sicard and Galezowski,[12] who reported a unilateral Argyll-Robertson pupil occurring in a case of syringomyelia. Mydriasis commonly found in cerebral syphilis is likewise found in general paresis, and anisocoria is seen in all types of syphilitic disease of the central nervous system, but neither is pathognomonic. Disease of any of the other cranial nerves has been observed in all types of syphilitic involvement of the central nervous system. The tendon reflexes may be lost or increased again, dependent upon the localization of the process. Transitory or permanent amaurosis, aphasia and hemiplegia, are common both in general paresis and cerebral syphilis, hemiplegia likewise not infrequently being a complication of tabes.

Epileptic convulsions, focal or diffuse, are seen in syphilitic meningitis, cerebral syphilis, and general paresis, Marinesco and

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[8] Lancet, 1881. 95.

[9] Revue Societe de Neurologie, June, 1910.

[10] Neurologische Centralblatt, May 16, 1914.

[11] Revue Neurologique, July 30, 1913, 105.

[12] Ibid.

Minea[13] recently reporting a case of general paresis dying during epileptic convulsion, and Nonne two cases in which epilepsy preceded tabes dorsalis. To the pain due to tabetic root lesions we have a simile in the cephalgias frequently observed in general paresis and cerebral syphilis, and so long considered to be of increased nocturnal severity in character. Considering the diffuse lesions of general paresis the changes of character and the psychical manifestations exhibited by these patients is not to be wondered at; but one frequently sees similar phenomena in cases showing evidences of focal involvement, and the severity of the symptomatology is not always indicative of the extent of the process in the nervous tissue, it being frequently impossible to pronounce beforehand a marked or slight, diffuse or focal, anatomical involvement. The stand of M. Nonne is indeed somewhat obscure, as is shown in his conclusions of a case presenting symptoms of neurasthenia with periods of depression: The serological examination in this case showed the Wassermann test to be positive on the blood and spinal fluid, with a lymphocytic count of 33/3 in the spinal fluid. The microscopic findings were infiltration of the pia mater and of the vessel sheaths of the small vessels in the cord and cerebral cortex with round cells and a few plasma cells, and the changes in the nervous tissue were distinctly focal in character. He asks, "Was one justified in diagnosing this a case of cerebral syphilis? on this depending upon what we until now, and as I myself mean, clinically considered as cerebral syphilis, my answer is No, for we have here no symptomatology of localized syphilitic changes, but, on the contrary, in a clinical sense, only evidence of diffuse involvement."

Of the manifestations due to the loss of the cortical inhibitory control commonly observed in the diffuse lesions of general paresis we also find evidences in the more localized changes of cerebral syphilis, and trophic disturbances may be observed in any syphilitic involvement of the central nervous system.

Just as it has been shown that the Treponema pallidum is the causative agent of the early and late manifestation of syphilitic disease of the body, so also is it found that the characteristic reaction produced irrespective of location or time of involvement consists in a perivascular infiltration of mononuclear lymphocytes and plasma cells with proliferation of the walls of the affected vessels and subsequent degeneration of the surrounding tissue, due either to the presence of the organism itself or to the metabolic changes resulting from the disturbed vascular condition. The ultimate result of the presence of the organism in the nervous system being a neuronic degeneration, whether of the spinal sensory neuron, as in tabes, the cortical association neuron, as in general paralysis, the visual neuron, as in primary optic atrophy, the upper motor neuron, as in primary lateral sclerosis, or the lower motor neuron, as in progressive muscular atrophy. The miscroscopic findings today generally considered as diagnostic of general paresis are those of a diffuse parenchymatous syphilis with loss of tangential fibers, neuroglia overgrowth, infiltration of the sheaths of the smaller vessels, with mononuclear lymphocytes and plasma cells, possible disturbance of the cortical lamellation, and occasional focal exacerbations. Cerebral syphilis or mesoblastic syphilis is considered to be either vascular, meningeal, or gummatous.

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[13] Reunion Biologique de Bucrest, Mars 6, 1913.

In an examination of the pathological material of fifty-three cases, including tabes, tabo-paresis, general paralysis of the insane, cerebral syphilis, and syphilitic meningitis in the Laboratory of Neuropathology of the University of Pennsylvania, I was impressed by the similarity of the pictures. In all one finds to a greater or less extent an infiltration of the meninges and the sheaths of the smaller vessels of the central nervous system by mononuclear lymphocytes and plasma cells, and further, this infiltration in general paresis does not confine itself to the vessel sheaths or in cerebral syphilis to the surface of the central nervous system. In considering the degree of degeneration of the nerve cells, one must realize that he is dealing with a variable quantity and not too freely describe diminution or loss of the nerve cells. Of the chromophilic granular changes of the cells, one frequently finds most pronounced focal changes in general paralysis, and not infrequently severe symptomatic evidence of general paralysis and cerebral syphilis, with little or no changes in the granular cellular arrangement. A disturbance of cortical lamellation is seen only in severe advanced cases and consequently can not be pathognomonic. In considering a loss of the tangential fibers and glial overgrowth one is again dealing with the relative. Not uncommonly in either general paralysis or cerebral syphilis there is a pronounced lack of correlation between the symptomatic and microscopic findings. It may be possible that the explanation why some alienists can so readily diagnose between general paralysis and cerebral syphilis may lie in the fact that patients with early or intermediate states rarely find admission to insane hospitals, and their experience has been gained chiefly from advanced types.

Just as the causative agent and the tissue reaction in syphilis of the central nervous system are similar, so also are the laboratory findings in the serological tests, the characteristic findings in the spinal fluid being a lymphocytosis and an increase of the globulin and albumin. It was at one time held that the Wassermann test was alike positive on the blood serum of general paresis and cerebral syphilis, but was as frequently negative on the cerebrospinal fluid in cerebral syphilis as positive in general paresis, and further, that marked lymphocytosis was more frequently found in cerebral syphilis. Nonne[14] makes the following statement: "In general paresis the Wassermann on the blood serum is positive in 100 per cent. of the cases; on the cerebral spinal fluid using 0.2 c.c. of the fluid in 90 to 95 per cent., and using 1 c.c. in a 100 per cent., phase 1 is positive in 95 to 100 per cent. of the cases. In cerebral syphilis the blood serum is positive in 70 to 80 per cent. of the cases; on the cerebral spinal fluid by the original method in 20 per cent. of the cases, and by Hauptmann's method in 100 per cent. phase 1 is always positive." Feldes and McIntosh[15] state: "A positive reaction in the fluid indicates a syphilitic lesion of the central nervous system. In active untreated cases of dementia paralytica, tabes dorsalis, and cerebral syphilis the reaction is positive both in the serum and cerebral spinal fluid. In cerebral syphilis without involvement of the spinal cord the cerebrospinal fluid is negative. Except in the latter cases the strength of the reaction has no certain diagnostic value. The reaction is apt to be negative in the serum or cerebrospinal fluid in the cases of hemiplegia, non-progressive tabes dorsalis, and old lesions of the nervous system, especially in cases of stationary congenital syphilis." Kirchberg[16] found in an examination of one hundred cases of general paretics the Wassermann reaction to be positive on the fluid in 78 per cent. of the cases and on the blood in 93 per cent. He concluded that the diagnosis of general paralysis should never be excluded because of a negative Wassermann reaction, and inasmuch as eleven of the twenty-two cases showing negative Wassermann were tabo-paretics, the Wassermann reaction could no longer be used as a differential point between tabes and general paresis. Mitchell, Darling, and Newcomb in an examination of the lymphocytosis of the spinal fluid in clinical cases of syphilis of the central nervous system found counts as high as 120 and as low as 0 in cases of general paresis.

I wish to express my thanks to Dr. William G. Spiller for placing the above material at my disposal and for many kind suggestions in the preparation of this paper.

PERMANENT PARTIAL COMPRESSION OF BOTH COMMON CAROTIDS IN EPILEPSY: A REPORT OF EIGHT OPERATIONS.

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Ligation of the large afferent vessels of the brain for the relief of epilepsy is not a new procedure. Although such operations have never received anything approaching general recognition, one may find in a search of the literature embracing the last few decades record of many instances of ligation of one or more of the large arteries of the neck in epileptics.

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[14] Diagnose and Therapie der Syphilogenen Erkrankungen des Zentralnerven Systems.

[15] Brain, 1913, xxxvi, 193.

[16] Archiv f. Psych. u. Nerven., 1914.

Baracz,[1] Sommer,[2] Binswanger,[3] Wyeth,[4] Hasse,[5] and Alexander[6] have mentioned the favorable effect upon general epilepsy which may be induced by ligation of the carotids or vertebrals. Many years ago Wyeth observed that "since dilatation of the arterioles and capillaries of the medulla oblongata is accepted by Schroeder, van der Kolk, Neimeyer, and others as the most constant lesion in epilepsy, I would suggest, and would perform if the opportunity presents, deligation of both vertebral arteries. This would arrest the direct and probably irritating flow of the blood through this ganglion, leaving the recurrent flow from the carotids through the posterior communicating arteries to supply the necessary amount of nutrition to this portion of the encephalon."

Alexander, of Liverpool, ligated the vertebral arteries in epilepsy with what seemed at first to be excellent effect, but later reported this method to be without value (Binswanger and Momburg). The investigations of Ritters[7] sought to explain the failure of veretebral ligation. They apparently made clear that the vertebral arteries play an unimportant role in the blood supply of the brain. The carotids, according to Ritters, conduct almost all of the blood to the brain.

Delegeniere[8] observed excellent results in a case of epilepsy following ligation of the superior longitudinal sinus just above the torcular Herophili. During a trephining it became necessary to ligate the longitudinal sinus to prevent hemorrhage. Delegeniere regards epilepsy as a clinical syndrome common to many pathological conditions, and holds that the many causative lesions of epilepsy produce in different ways a permanent dilatation of the veins upon the surface of the cerebral hemispheres. He, therefore, regards it a logical step to modify the venous circulation of the cortex by ligation of the terminal portion of the longitudinal sinus in the belief that distention of the superficial cerebral veins is the cause of irritation of the cortex. He regards this operation as analogous in its purpose and mode of action to ligation of the upper part of the internal saphenous vein for varicosities of the veins of the leg, that is, placing a ligature around the longitudinal sinus would, he says, bring about a collapse of the overdistended veins which supply the sinus.

Jonnesco, von Jacksch, Spratling and Park, Joseph Beck, and a number of others have performed cervical sympathectomy in general epilepsy with a view to cutting off sensory stimulation from the viscera and especially to influence directly the circulation of the brain by changes in the caliber of its bloodvessels through the action of the vascular nerves.

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[1] Wien. med. Wchnschr., 1889

[2] Virchows Arch., 1890, cxix, 2, 362.

[3] Die Epilepsie.

[4] Essays in Surgical Anatomy.

[5] Krankheiten des Nervensystems, 297.

[6] Gowers, Dis. of Nerv. Sys., vol. ii.

[7] Verh. d. Ges. f. Chir., 1913.

[8] Arch. Prov. de Chir., 1914, No. 10.

Lafforgue[9] observed in rabbits as a direct result of stimulation of the cervical sympathetics, spasmodic ischemia of the whole cerebrum, cerebellum, and medulla oblongata.

Jonnesco concluded that the cervical sympathetics contained vasoconstrictor fibers for the head, face, and heart. This was made evident by electric excitation. What is more important in this connection, Jonnesco further noted that the cervical sympathetics contained vasodilators for the inner part of the cheeks, gums and lips and for the brain. This was shown by the application of feeble currents.

Winters' table shows that of 122 cases of general epilepsy, treated by cervical sympathectomy, 6.6 per cent. were cured, 13.9 per cent. were preliminarily cured, 18.9 per cent. improved, 54.9 per cent. not improved, and 5.7 per cent. died.

The pathogenesis of epilepsy is obscure, and we are still ignorant of the cause of the attack. Many writers consider it unlikely that a palpable anatomical alteration exists. Orloff[10] found no characteristic changes except thickening of the glia, especially in Ammon's horn, possibly a congenital sclerosis.

The claim of Chaslin that a gliosis is to be regarded as the cause of epilepsy is, as stated by Hirt, by no means proved. Much more plausible is the theory that the amount of blood in the brain is of some importance in this connection.

Turner[11] says that the exciting cause of epileptic attacks is a sudden stasis in the blood stream, usually in a limited portion of the cortex.

Bechterew believes that there is an increased blood flow to the brain and a temporary dilatation of the capillaries during the attack. Bechterew's views were based upon the experiments of Todorsky.[12] On the other hand, von Leyden and Sommer noted evidence that the exciting cause of the epileptic attack is anemia of the brain. The former observed epileptic attacks in cases of aortic stenosis undoubtedly as the result of a temporarily insufficient blood supply, and the latter remarked their occurrence in a case of ankylosis of the atlas which had produced narrowing of the vertebral canal in its upper portion.

It has been observed that sodium santoninate injected into rabbits quickens the pulse and respiration. The rabbits' ears become redder and hotter, due to the increased blood supply. This is followed by fine fibrillary contractions. With larger doses, convulsions appear with clonic spasmodic movements followed by return to the normal. Jelliffe[13] found in rabbits thus injected with santonin, intense conjestion of the meninges and of all the cerebral vessels, large and small.

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[9] Quoted by Spratling and Park, Jour. Nerv. and Ment. Dis., April, 1914.

[10] Archiv. f. Pschiatrie and Nerven Krankheiten, vol. xxxviii, Heft 2.

[11] Jour. Mental Science, vol. liii, No. 220.

[12] Hirt, Diseases of General Nervous System, 586.

Permanent narrowing of both common carotids was adopted by Momburg[14] for the relief of epilepsy in 2 cases. Coming accidentally upon an epileptic during a seizure in the street, it occurred to him to apply digital compression to both carotids to determine the effect of such compression upon the typical clonic contractions which were present. With thumb and forefinger he compressed both common carotids and almost immediately the convulsive movements ceased, the man drew a deep breath, opened his eyes, looked about, and seemed to be conscious. While being carried into a neighboring house the convulsions reappeared, but compression of the carotids with both thumbs again caused the contractions to cease and consciousness to return.

Epileptic convulsions had previously been controlled through digital compression by others. Binswanger speaks of it in his work on epilepsy as having been recommended by von Reimer in the middle of the last century, and later by Corning. Hasse, according to Momburg, regarded the procedure as difficult, and had observed no successful trials of it. At the suggestion of Momburg, Volland was successful in several instances in controlling epileptic attacks by digital compression of the carotids. He observed, as did Hasse, that it is not always easy thus to compress the carotids, owing to the thick neck musculature and the deep position of the vessels. My colleague at the Indianapolis City Hospital, Dr. Will C. Moore, succeeded in arresting the attack in a single instance by digital compression of the carotids.

Momburg permanently narrowed the common carotids in 2 cases with silver wire loops, proceeding from the convenient hypothesis that in epileptics the seat of the disease is represented by the entire brain, and may be looked upon as an abnormal state of irritability, and that this irritability may be decreased by decreasing the blood supply and by decreasing the nutrition to lower the irritability of cells without effecting the vitality of such cells.

Momburg operated under novocain suprarenin anesthesia, compressing both carotids by twisting the crossed ends of a silver wire loop until the temporal pulse became barely perceptible on the corresponding side. He operated on 2 cases, one in February and one in March, 1914. Distinct improvement followed in both instances. His published article in the *Deutsche medizinische Wochenschrift* appeared within less than two months after the first operation and within one month after the second. It need hardly be said that a report made so soon after such an operation must be looked upon as of somewhat doubtful value for several reasons, two of which are that sufficient time did not elapse for the development of compensatory dilatation of the other vessels and establishment of collateral circulation, and that such temporary beneficial results will, as has been noted frequently by neurologists, follow the performance of almost any operation upon an epileptic.

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[13] Jour. Mental and Nerv. Dis., 1909, p. 252.

[14] Deutsch. med. Wnschr., April, 1914.

During August, 1914, I compressed both common carotids in 2 cases of general epilepsy, the plan followed being in most respects that adopted by Momburg. I did not employ local anesthesia in the first case for the reason that the attacks were so frequent, occurring as often as seven times a day, that I feared the onset of an attack might lead to a serious surgical accident. Silver wire, 1 mm. in thickness, was passed under each common carotid, a short loop was cut off, and the ends were twisted until the temporal pulse on each side became so slight as to be just perceptible. A catgut strand was tied to the twisted ends of the wire and left hanging out of the wound to be used as a guide in case threatening cerebral symptoms should require immediate removal of the wire. With the catgut strand the wire loop can be drawn up into the wound and snipped off with blunt-end scissors quickly and without anesthetic of any kind.

Of these two first cases, one was in a young man, aged twenty years, who had suffered five or six attacks of the grand mal type daily. The other case was that of a girl, aged seventeen years, whose attacks, though much less frequent, were also of the severer form. Partial compression of both common carotids produced in neither of these cases any untoward effects. Both patients slept soundly, as might have been expected in view of the decreased blood supply to the brain, for about eighteen hours. In both cases the result although gratifying, so far as the effect upon the frequency and character of the attacks is concerned, left much to be desired. The young man, though distinctly benefited, has had since the operation attacks of petit mal, in the average, one and one-half times a week. During the last month he has had but two attacks. Previous to operation the attacks, as stated above, occurred several times daily and were of severer form. In the case of the young girl, there has been a slight increase in the length of the interval between the attacks, and the character of the epilepsy has been changed for the time at least from grand mal to mild petit mal.

In the first week of November, 1914, I narrowed both common carotids with silver wire after the plan described above in two additional cases. One was a case of petit mal in a man, aged thirty-five years, the other a case of grand mal of the severest character and of long-standing in a woman, aged forty-six years. The man, of thirty-five with petit mal was apparently somewhat improved in that the interval between attacks was more than doubled in length. The severity of the attack was reduced. The result in the case of a woman of forty-six with grand mal was a complete failure. She developed coma immediately following the operation and the silver wire loops were removed, one within twenty-four hours after operation and the other four days later. Upon gradual recovery from the coma during the next two or three days following operation a complete hemiplegia of the right side made itself manifest with aphasia, from which the patient is now slowly recovering.

January 10, 1915, I operated on a fifth case in the manner described. The patient was a man, aged thirty-three years. He had suffered daily severe attacks following a blow upon the head over the upper Rolandic area on the right side. A decompression had been made without benefit. In the period of seven weeks elapsing since the carotids were compressed he had had no attacks whatever. Since such a short period of respite may follow any imaginable operation upon an epileptic, such a temporary improvement may be said to be without great significance.

The sixth case was operated March 6, 1915, the patient being a male negro, aged twenty-seven years. For one year he had suffered attacks of grand mal at intervals of nine days with almost continuous headaches. During the last few months prior to operation the attacks had increased in severity and frequency. Between the date of the operation and April 18 there have been but two attacks, one of petit mal, on March 11, and one of grand mal, on April 10.

Momburg remarks that his results indicate with what safety the blood supply to the brain may be decreased. This is, I believe, slightly misleading, notwithstanding it is frankly added that two observations cannot suffice for the drawing of general deductions. The one serious brain complication in my experience might be attributed, of course, to faulty technique or injudicious case selection, yet it seems justifiable in view of the paucity of actual trials of carotid compression to say that except in youthful persons the sudden decrease in the blood supply to the brain may at any time, for aught we know, give rise to serious cerebral consequences. It should not be forgotten that the very factors upon which hope for success in carotid compression may be based, namely, the meager facilities for the establishment of collateral circulation of the carotis communis and the restriction of the vertebrals in their bony canals represent factors of danger if the blood supply to the brain be decreased too greatly by the compression.

It is unfortunate that in the case of the brain it is not easy to determine by any of the known tests of the efficiency of circulation precisely how much change is induced in the blood supply to the brain by compression of the carotids. Appreciating the great importance of such tests, the ignoring of which may lead to the incurring of serious and fatal errors in operations, one is nevertheless unable in the case of the common carotid to profit greatly by the employment of such tests. Matas,[15] writing of circulation tests, remarks that "The time has now come when every progressive surgeon must regard it as his obligate duty to investigate and ascertain, by actual tests, what the behavior of the peripheral circulation will be whenever an operation is contemplated in which the parent vascular trunk is liable to be involved. This is no longer a matter of academic or theoretical interest, but a subject of practical, vital importance in the treatment of such cases.

The Pachon blood-pressure method, the test of the venous turgescence, the calorimetric test, and other methods of great value in determining the efficiency of the circulation in the extremities after occlusion of the large trunks are of doubtful practical usefulness in the case of the brain in comparison with the simple expedient of determining the strength of the pulse in the temporal artery. The excellent methods of Matas, particularly that of applying temporarily the aluminum band as a test of efficiency of circulation, would be of greater value in the cases under consideration were it not that the sleep which is probably consequent upon the decreased blood supply to the brain may mask cerebral symptoms which otherwise would give warning of danger

In dogs, both common carotids and one vertebral have been ligated without fatal result, and in man, both common carotids have been ligated, one at a time, with only two weeks elapsing between the operation on the two sides. Stiles gradually occluded both carotids in hydrocephalus, two weeks elapsing between the beginning and the end of the occlusion. J. P. Lord and Frazier have also followed this gradual but complete occlusion plan in hydrocephalus with success, and Fenger[16] completely ligated first one common carotid and then the other with an intervening period of a few hours, and with favorable results.

Dr. E. H. Beckman,[17] of the Mayo Clinic, in a case of aneurysm of the inside of the skull involving the right lateral sinus associated with aneurysm of the left internal carotid artery, ligated at one operation the left common carotid just below the bifurcation and the right external carotid artery. The right and left internal jugular and the left external jugular veins were also ligated. The patient made an uninterrupted recovery and was relieved of pain and throbbing sensations in the head.

The favorable postoperative histories of the cases cited above indicate in what surprising degree the blood supply to the brain may be reduced in certain cases. However, it is by no means established that even gradual or partial occlusion of one common carotid is entirely free from danger of consequent cerebral mischief and it need hardly be stated that partial occlusion of both carotids should be done with caution.

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[15] Jour. Am. Med. Assn., October 4, 1914.

[16] Ricketts, Surgery of the Thorax.

[17] Trans. West. Surg. Assn., 1914.

Instances of compression of the common carotids for epilepsy are so few in number that general conclusions must, of course, be withheld. In view of the extremely unsatisfactory results of non-surgical treatment of general epilepsy the practice of the plan of compression of the common carotids may be considered justifiable, though the procedure at present should be regarded as an experimental one. Unfortunately, today, as centuries ago, we are reduced to the sad necessity of trying many uncertain remedies in epilepsy, trusting that at some time we may hit upon one that is truly efficacious. Certainly carotid compression cannot be considered appropriate in cases in which there is the slightest reason to suspect irritation in any peripheral zone inducing the attack until such peripheral irritation has been excluded. If the operation is worthy of future trial it is in cases of idiopathic general epilepsy, occurring in youthful persons or in traumatic or focal epilepsy which has persisted after cranial decompression, or other appropriate intervention. In such cases the operation may be done without great fear of serious consequences and with considerable hope of benefit.

The circumstance that in three of the six cases operated on by the writer the severity of the attack was reduced, suggests that whereas the increased influx of blood to the brain probably does not bear to the attack the relation of ultimate cause, nevertheless, the sudden influx of blood may determine in some manner the time and also the severity of the attack. Moreover, in view of the accredited fact that peripheral stimuli in almost any zone may induce epilepsy, it is believed that the suddenly increased influx of blood to the brain may represent the agent which activated by such stimuli makes the direct assault upon the cortex. Obviously an earnest effort to locate and correct any cortical lesion or an existing peripheral source of irritation, for example, in a stagnant colon should precede an attempt to reduce the aggregate caliber of the afferent bloodvessels of the brain in general epilepsy.

In conclusion, I desire to express my appreciation of valuable assistance rendered in the preparation of this report by my associates Doctors W. C. Moore and H. K. Bonn.

STATISTICS OF AGE MORTALITY BASED UPON THE NUMBER OF PERSONS ALIVE AT EACH AGE.

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PHILADELPHIA.

Various ways have been commonly employed to express the mortality from different diseases according to age. One method presents, for a given disease at a given age, the ratio of deaths at this age to the total number of all deaths from that disease irrespective of age. A second method gives for a specified disease at a given age the ratio of deaths at this age to the total number of deaths from all causes irrespective of age. A third method shows for a given disease at a given age the ratio of deaths at this age to the total number of deaths from all causes occurring at that particular age.

Useful as these methods are for furnishing certain kinds of information, there is a great deal that they do not tell which is revealed by still another method. This method expresses for a certain disease the ratio of the number of persons dying at each age to the whole number of persons alive at the same age; that is, the mortality from the disease for every 10,000 persons living at the particular age. This method furnishes something like an absolute standard. Such figures render one independent of such variable factors as the number of persons living at other age-periods, or dying at the other age-periods or from other diseases. These other factors may be entirely misleading as to the proportion of deaths from a disease among those living at any one age-period.

This is by no means a new method for expressing age mortalities, but is not as generally recognized and employed as it should be. It is often omitted in text-books and other places that have a great opportunity for diffusing knowledge.

The charts presented in this paper are compiled from the United States Census Reports for 1910. The figures presented could not be obtained directly from these reports, but had to be compiled from different volumes, one volume dealing with mortality statistics, which does not give the age mortality per 10,000 persons living at the same age, and the other volume dealing with population statistics. Only the mortality figures for the registration area of the United States have been used, which includes 58.3 per cent. of the total population of the United States. The population statistics for the whole country had to be reduced, therefore, to 58.3 per cent. of their amount, to correspond to the mortality statistics for the registration area.

In all the charts the *dotted* line represents the number of deaths for the disease specified for different decades per 10,000 persons living at corresponding decades, except in the pneumonia chart where this line indicates the mortality per 1000 living persons. The *solid* line represents the ratio of deaths from a particular disease at different decades to the whole number of deaths at all ages from the same disease. The *broken* line in Chart III represents the ratio of deaths from tuberculosis at any decade to the total number of deaths from all causes at the corresponding decade.

The figures at the upper part of the charts indicate the different decades.

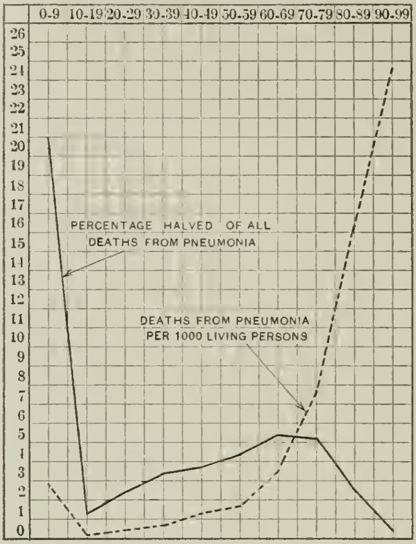

Chart I.—Pneumonia; all forms. Registration area of the United States.

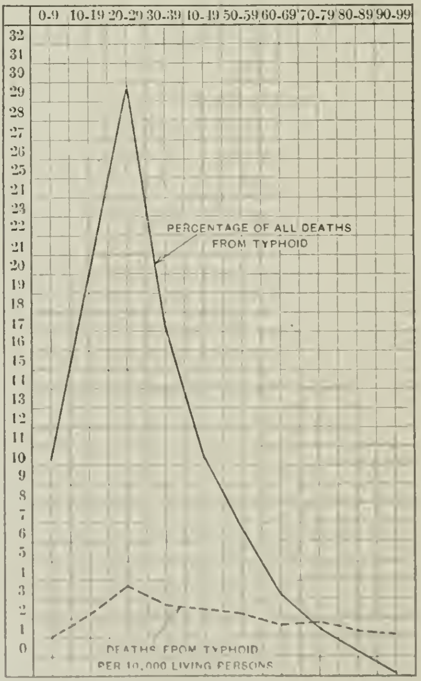

Chart II.—Typhoid fever. Registration area of the United States.

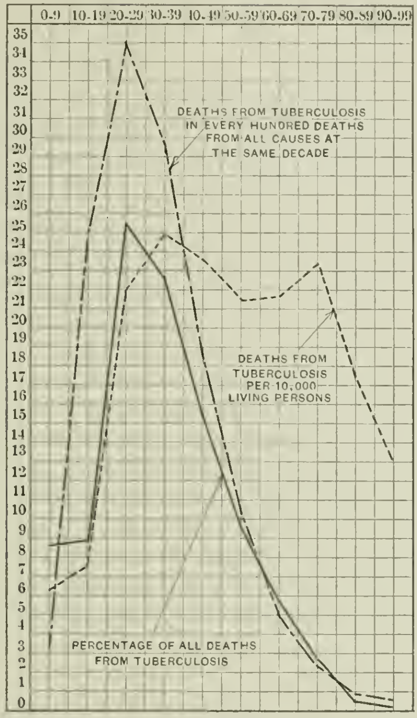

CHART III.—Tuberculosis; all forms. Registration area of the United States.

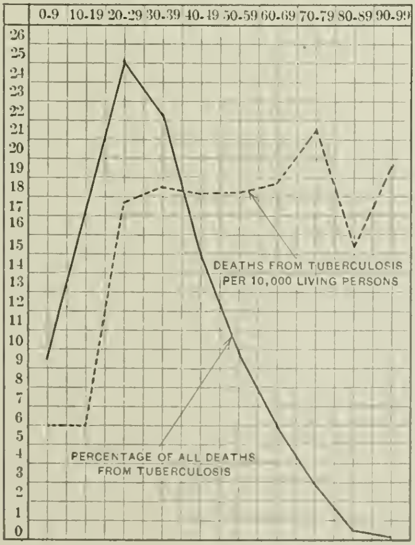

CHART IV.—Tuberculosis; all forms. Pennsylvania.

The figures to the left of the charts correspond to the points on different parts of the curves, and therefore indicate several things: (1) the number of deaths per 10,000 persons living at the specified decade except in Chart I, in which the mortality is expressed in terms of 1000 living persons; (2) the number of deaths due to the particular disease out of every 100 deaths at all ages from the same disease except in Chart I, where the percentage is halved, that is, should be doubled to give the proper percentages; (3) only in Chart III the number of deaths due to a given disease out of every 100 deaths from all causes at the same decade. Figures for those dying at an age over one hundred years or at an unknown age are not shown.

The charts deal with pneumonia, typhoid fever, and tuberculosis for the registration area of the United States, and with tuberculosis for Pennsylvania. Thus Chart I demonstrates how much more frequently persons die of pneumonia during later life, provided the mortality is based on the number of persons living at a corresponding age, and how misleading it would be to draw conclusions from the absolute number of deaths from pneumonia during the later decades. This chart also shows that while the proportion of deaths from pneumonia under ten years of age is high compared to all deaths from pneumonia at all ages, the large number of persons alive at this period materially reduces the relative prevalence of the disease at this decade.

Chart II reveals an interesting picture in regard to typhoid. The curve depicting the high figures for the decade twenty to twenty-nine corresponds to the average teaching that typhoid predominates markedly in youth and early adult life, this particular curve in the chart and the prevalent teaching on the subject being based upon the relation between the number of deaths from typhoid at this period and the total number of deaths from typhoid at all ages. The other curve in the chart shows the number of deaths from typhoid at each decade for each 10,000 persons living at the same decade, the contrasts in this curve being noticeably less striking than in the other curve.

Chart III pictures the mortality curve for all forms of tuberculosis in the registration area of the United States, and shows what has long been known, but is frequently overlooked, that tuberculosis continues unabated its extensive ravages even among elderly persons, though the absolute number of deaths from tuberculosis is actually diminishing. Among those who have emphasized the high mortality from tuberculosis among the aged are Wilson Fox and Cornet. A recent pamphlet issued by the Maryland State Department of Health, entitled "A Brief Review of the Tuberculosis Campaign, 1904–1914," shows that "in the white population beginning with the twentieth year of life all persons are equally liable to death from tuberculosis."

Chart III contains a third curve, not present in the other charts, representing the tuberculosis mortality at different decades in comparison to the total mortality from all diseases at corresponding decades.

Chart IV indicates the prevalence of tuberculosis in Pennsylvania at different ages, the mortality actually increasing in the decade seventy to seventy-nine. The figures given by Cornet indicate that for every 10,000 males between sixty and seventy years of age as many as 99.65 die of tuberculosis. German statistics frequently give a relatively higher mortality from tuberculosis among the aged than do the English figures.

Smaller divisions of the age-periods than decades will often furnish more important information. Thus we find for the registration area of the United States for pneumonia (all forms) 147.3 persons die under one year of age per 10,000 persons alive at this age, while the mortality at four years is only 6.7 per 10,000. Again, the mortality for diarrhea and enteritis under one year is 345.7 per 10,000 and at four years only 2.5 per 10,000.

Much more could be said on this subject, but I trust the one point it seemed worth while to specially emphasize has been made plain, that no figures satisfactorily express the frequency of the deaths from any disease at a given age unless they show the number of deaths from the disease for every 10,000 persons living at the same age.

CONCERNING THE PRESENCE OF TUBERCLE BACILLI IN THE BLOOD OF TUBERCULOUS PATIENTS.[1]

By Leo Kessel, M.D.,
NEW YORK CITY.

The results of numerous studies of this subject during the past ten years have shown a complete lack of agreement among the various investigators. Some authors claim to have demonstrated tubercle bacilli regularly by a direct microscopic examination of the blood of tuberculous patients and frequently by the inoculation of such blood into guinea-pigs and rabbits, while other workers in this field report constantly negative results when microscopic examinations were made and few or no positive results when animal inoculations were employed. A review of the earlier work has been given by Bergeron,[2] and the more recent literature was well reviewed by Ernest Fraenkel,[3] and in this country by Berry.[4] That tubercle bacilli are at times present in the blood in acute miliary tuberculosis was demonstrated by Weichselbaum,[5] Lustig,[6] Meisel,[7] and others. The occasional presence of tubercles in the spleen, liver, kidneys, and other organs of patients who have died of chronic pulmonary tuberculosis indicates that at times tubercle bacilli gain access to the circulation. Weigert[8] emphasized the fact that pulmonary tuberculosis in contrast to acute miliary tuberculosis was not to be considered a general infection, and his views were until recently regarded as a fundamental truth in the pathology of human tuberculosis.

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[1] This work was carried out in the wards and laboratories of the Montefiore Home and Hospital for Chronic Diseases.

[2] Etude critique sur la presence du bacille de Koch dans le sang, Thèse, Paris, 1904.

[3] Schmidt's Jahrbucher, March, 1913, cccxvii, Hft. 2, 201.

[4] Tubercle Bacilli in the Blood, Jour. Inf. Dis., 1914, xiv, 162.

During the past ten years many authors have claimed, upon the basis of their investigations, that in cases of chronic pulmonary tuberculosis, tubercle bacilli are often present in the blood even in the incipient stage of the disease (Kennerknecht,[9] Kurashige,[10] Jessen and Rabinowitsch,[11] and Liebermeister,[12] while others state that they have found the organism in the blood of clinically healthy persons (Suzuki and Takaki,[13] Rumpf[14]). Kennerknecht and Kurashige insist upon the existence of a primary bacillemia in tuberculous infections.

In order to determine the presence of tubercle bacilli in the circulation, two main methods have been pursued. Those workers who have relied upon one of these—namely, the microscopic examination of the blood—have reported results varying from 0 per cent. to 100 per cent. positive findings. At first, simple blood smears or the inoscopic method of Jousset[15] were employed for microscopic examination; then the antiform and the acetic acid method of blood examination (Staubli[16]), and finally the Schnitter[17] method was generally adopted. There have been several modifications of this last method by various investigators; all, however, are fundamentally similar. The pitfalls encountered in the microscopic methods elaborated to determine the presence of tubercle bacilli in the blood are many, and so misleading as to cast doubt upon the reliability of the positive reports by microscopic examination. Thus, distilled and tap water have been found by Beitzke[18] and Brem,[19] respectively, to contain acid-fast organisms. The stroma of red-blood corpuscles, lecithin, and cholestrin are acid-fast, and may, as Maixner[20] has shown, be mistaken for tubercle bacilli. Flakes of fibrin (Kahn)[21] and red-colored crystals (Lange and Lindemann)[22] may similarly lead to error. Anyone who has examined antiformin blood sediment stained according to the Much method for granules will, we believe, readily grant that the definite identification of tubercle bacilli is difficult and that the possibility of error is considerable; and finally it has long been known that organisms other than the tubercle bacillus, existing in our environment, may be acid-fast and that saprophytic bacteria occasionally acquire an acid-resistant power.

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[5] Tuberkelbacillen im Blute bei allgemeiner akuter miliar Tuberkulose, Wien. med. Wochenschr., 1884, No. 12, 334.

[6] Ueber tuberkelbacillen im Blute bei an allgemeinen akuter miliar tuberkulose Erkrankten, Wien. med. Wochenschr., 1884, No. 48, 1430.

[7] Vorkommen von Tuberkelbacillen im Blute bei allgemeinen akuten miliar tuberkulose, Wien. med. Wochenschr., 1884, No. 48, 1429.

[8] Neue Mittheilungen über Pathogenie der acuten allgemeinen miliar Tuberculose, Deut. med. Wochenschr., 1883, No. 24, 349.

[9] Ueber das Vorkommen von Tuberkelbazillen im Strömenden Blut bei Kindern, Beiträge z. klin. d. Tuberkulose, 1912, xxiii, 265.

[10] Ueber das Vorkommen des Tuberkel Bacillus im Strömenden Blut der Tuberkulosen, Zeitschr. f. Tuberk., 1911, xvii, Hft. 4, 347.

[11] Ueber das Vorkommen von Tuberkelbacillen im Kreisenden Blute und die praktische Bedeutung dieser Ersheinung, Deut. med. Wochenschr., 1910, No. 24 1116–1118.

[12] Ueber "Secundare" Tuberkulose, Med. klin., 1912, No. 25, 1018–1022.

[13] Ueber die Beziehung zwischen der von Pirquetschen Reaction und den Tuberkelbacillen im Blut, Centralbl. f. Bacterial, Orig., 1911, lxi, 149.

[14] Ueber das vorkommen von Tuberkelbacillen im Blutstrom, Münch. med. Wochenschr., 1912, No. 36, 1951.

[15] Nouvelle Methode pour isoler le bacille de Koch des humeurs de l'organisme, La semaine médicale, 1903, No. 3, 22.

[16] Beiträge zum nachweis von Parasiten im Blut, Münch. med. Wochenschr., 1908, No. 50, 2601.

[17] Nachweis u. Bedeutung der Tuberkelbacillen im Strömenden Blut, Deut. med Wochenschr., 1909, No. 36, 1566.

The other method which has been employed is that of animal inoculation, and for this purpose the guinea-pig has been the animal commonly used. That this animal is susceptible to infection with tubercle bacilli is a well-established fact, and while some investigators who claim advantages for the microscopic method have stated that the guinea-pig is not sufficiently sensitive, it has been shown by Selter[23] that ten tubercle bacilli suffice to inoculate a guinea-pig successfully, and Fraenkel and Baumann[24] think that this can be accomplished with a single organism. In order to avoid the possibility of using guinea-pigs previously inoculated with tuberculosis a preliminary tuberculin test can be made. It is probably true that all guinea-pigs are not equally susceptible to tuberculous infection (Markl),[25] and that some possess protective substances against tubercle bacilli (Kraus and Hofer);[26] but in a large series of experiments this becomes a factor of minor importance. It has been urged that the results of animal inoculation were negatived by the bactericidal action of the injected blood, but Anderson[27] was able to show that this bactericidal action if present was slight by adding a small amount of emulsion of tubercle bacilli to the citrated blood from one of his cases by inoculating a guinea-pig and readily producing tuberculosis. Moreover, Moewes[28] has shown that the bacillemia present in tuberculous guinea-pigs could be demonstrated by inoculating the blood of these animals into other guinea-pigs and producing tuberculosis, and Rautenberg[29] has performed similar experiments with monkeys.

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[18] Eine Fehlerquelle bei der Antiformin methode, Berlin. klin. Wochenschr., 1910, No. 31, 1451.

[19] Investigation of Blood for Tubercle Bacilli, Jour. Amer. Med. Assoc., 1909, liii, 909.

[20] Quoted in Zeitschr. f. Tuberculose, 1914, xxii, Hft. 3, 267.

[21] Zum Nachweis der Tuberkelbazillen im Strömenden Blut, Münch. med. Wochenschr., 1913, No. 7, 345.

[22] Ueber Tuberkelbacillen im Strömenden Blut, Centralbl. f. Bacterial. Ref., 1913, 57 Beiheft, 285.

[23] Vortag auf d. Niederrhein Ges. f. Natur u. Heilk., Bonn, July, 1913.

[24] Zeitschr. f. hyg. u. infections Krankh., 1913, lxxvi. Hft. 1.

[25] Beiträg zur Kenntnis der Nagana infection bei Meerschweischen, Centralbl. f. Bacterial, 1904, xxxvii, 530.

[26] Ueber auflösung von Tuberkelbacillen im Peritoneum gesunder u. tuberkulosen Meerschweinchen, Deut. med. Wochenschr., No. 26, 1227.

The argument has been advanced that the many negative results with animal inoculation could be traced to the treatment of the blood with antiformin before inoculation; this, it was held, destroyed the tubercle bacilli or so diminished their virulence that the inoculated animal could successfully withstand the infection.

Unlenhuth[30] has shown that a tuberculous sputum would yield positive inoculation results even after twenty-four hours' treatment with 20 per cent. antiformin, and Seemann[31] demonstrated that a 15 per cent. antiformin solution could not kill the tubercle bacilli in one hour. In view of these experiments, and considering the fact that, under ordinary circumstances, a clear solution is obtained by the antiformin method in twenty minutes to half an hour, it is unlikely that this method influences the virulence of the tubercle bacilli.

Our experiments were undertaken with the hope of determining whether a bacillemia existed in patients suffering from chronic pulmonary tuberculosis, and at the same time to confirm or disprove the value of the methods recently advocated for this purpose.

The methods which we pursued were as follows:

1. The blood taken from patients with advanced pulmonary tuberculosis was inoculated directly into the peritoneal cavities of guinea-pigs.
2. The blood from some of these patients was treated and examined microscopically.
3. The blood from tuberculous patients who had previously received an injection of tuberculin was inoculated intraperitoneally into guinea-pigs.
4. The blood was withdrawn from tuberculous patients who had previously received a tuberculin injection, and after removal of the serum intraperitoneal injections were made into guinea-pigs.

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[27] Bull. No. 57 Public Health and Marine Hospital Service of the United States, September, 1909.

[28] Tuberkelbacillen im Blute, Deut. med. Wochenschr., 1914, No. 10, 491.

[29] Zur Frage der Bacillaemie bei Tuberkulose, Deut. med. Wochenschr., 1914, No. 10, 492.

[30] Antiformin, Ein Bacterienauflösen des Desinfectionsmittel, Zentralbl. f. Bakt., 1908–1909, Abt. 1, Referate, xlii, 62.

[31] Die Braubarkeit des antiformins zum Nachweis von Tuberkelbacillen, Berl. klin. Wochenschr., 1909, No. 14, 628.

5. The blood, after removal of the serum, was planted upon culture tubes of gentian-violet media.

The technique pursued was as follows:

Method 1. With aseptic precautions 5 c.c. of blood were withdrawn from a vein at the elbow into a syringe. The blood was immediately injected into the peritoneal cavity of a guinea-pig whose ventral surface had previously been shaved and treated with iodin. This direct and rapid transferrence of blood rendered the use of citrated solutions unnecessary; intraperitoneal injections were made because this route had yielded satisfactory results in the hands of other investigators. Blood withdrawn from thirty-eight patients was examined by this method. Tubercle bacilli were found in the sputum of thirty-seven of them, and in the remaining patient definite bilateral pulmonary signs were present. The patients were classified according to the classification adopted by the Association for the Study and Prevention of Tuberculosis. One patient was in stage I, seven patients were in stage II, and thirty were in stage III, and of the last mentioned, many were acutely ill with high fever, chills, sweats, and the clinical manifestations of cavitation.

Of 38 guinea-pigs inoculated in the manner described above, 2 died forty-seven days, 1 fifty-eight days, 1 sixty-six, and 1 eighty-three days following the injection, and were autopsied. The remaining 33 animals were chloroformed at periods varying from sixty-three to one hundred and twenty-nine days following the inoculation. Careful autopsies were also performed upon each of these animals, and material was taken from the lungs, liver, spleen, and kidneys for microscopic examination.

The autopsies and microscopic examination failed to reveal the slightest evidence of tuberculosis in the inoculated guinea-pigs. In none of the animals was there any enlargement of either the mesenteric or retroperitoneal lymph glands, so that the occurrence of a mild tuberculous infection from which the guinea-pig recovered cannot here be considered as evenly remotely possible.

Method 2. The blood of ten patients (Nos. 19, 20, 21, 22, 23, 24, 31, 32, 33, 34) in whom the disease was far advanced was withdrawn for microscopic examination. The method of treating the blood was exactly the same as that employed and advocated by Klemperer,[32] and by which he had obtained positive results. Five c.c. of blood were withdrawn with aseptic precautions by a sterilized syringe which had been washed with distilled water. The blood was then transferred to a vessel which had been cleaned with soap suds, alcohol, and ether, cotton plugged and sterilized at 180° to 200° F. for one hour. To this 5 c.c. of blood, 10 c.c. of 3 per cent. acetic acid, prepared with distilled water, were added, the vessel being carefully shaken, without producing foam and then allowed to stand half an hour. This solution was poured into two centrifuge tubes, which had been cleaned in a similar fashion to the first used vessel, and were passed through a flame just before being used, and centrifuged for half an hour. The supernatant fluid was taken off and five times the quantity of 33 per cent. antiformin added. The centrifuge tubes were closed with sterile rubber corks and shaken until the fluid became clear. Then the tubes were filled with double distilled water and centrifuged for one hour (2500 revolutions to the minute). A small white sediment remained; the supernatant fluid was removed, the sediment washed with double distilled water, and centrifuged for one and a quarter hours. This washing and centrifugalization were repeated four times. The sediment from each tube was finally poured onto two new slides. The slides had been washed in alcohol and sterilized at 250° F. for one hour and glowed over a Bunsen flame just before use. This preparation was placed in a sterile Petri dish and dried in an oven, and finally stained with a freshly prepared Ziehl-Nielsen stain. The stain was made up with distilled water. A careful systematic search was then made of the blood which had finally been deposited upon the two slides. At least four hours were devoted to the examination of each one of the slides from these ten cases. Not a single tubercle bacillus was found.

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[32] Tuberclebacillen im Blut, Zeitschr. f. klin. Med., 1914, clxxx, Hft. H. 2.

The negative results obtained with methods 1 and 2 induced us to attempt method 3, which concerns itself with the inoculation into guinea-pigs of blood from patients who had some hours previously received an injection of tuberculin. Such an injection of tuberculin has been followed, it has been stated, and then again denied, by a mobilization of tubercle bacilli in the circulation.

Bacmeister[33] inoculated the blood of fifteen patients, who had previously received a diagnostic tuberculin injection, into rabbits and produced tuberculosis in four instances. Mayer[34] studied sixteen tuberculous patients who had received tuberculin injections, but the blood from these patients inoculated into guinea-pigs failed to produce tuberculosis, while Liebermeister[35] obtained positive inoculation results after a tuberculin injection where these had previously been negative. The latter has also seen a previously positive inoculation yield negative results following a tuberculin injection; he doubts whether tuberculin in the usually employed dosage can cause a mobilization of tubercle bacilli.

Rabinowitsch and Moewes[36] found more positive inoculation results in tuberculous guinea-pigs after a tuberculin injection than before, while Hage[37] failed to obtain positive inoculation results in tuberculous guinea-pigs regardless of how irregularly or systematically the tuberculin had been administered.

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[33] Des auftreten virulenter Tuberkelbacillen im Blut nach der diagnostischen Tuberculin Injection, Münch med. Wochenschr., 1913, No. 7, 343.

[34] Ueber das Vorkommen von Tuberkelbazillen im Strömenden Blut u. in der menschlichen Milch, Zeitschr. f. Tuberculose, 1913, xxi, Hft. 5.

[35] Sitzungsber. d. neiderrh. Gesells. f. Natur u. Heilk, Bonn, January 20, 1914.

[36] Sitzung. der Berliner med. Gesellsch., February, 1914.

Method 3. Seven patients (Nos. 36, 37, 38, 39, 40, 41, and 42), of whom five were in the third stage and two were in the second stage of the illness, were subjected to a tuberculin injection; 0.1 milligram or 0.2 milligram of Koch's therapeutic tuberculin was injected subcutaneously; seven hours later 5 c.c. of blood were withdrawn for direct inoculation into the perioneal cavity of a guinea-pig. Of these seven guinea-pigs, one died on the thirty-eighth day following inoculation and was autopsied, while the others were chloroformed at periods ranging from sixty-seven to ninety-one days. After the inoculation, careful autopsies were performed and material taken from the various organs for microscopic examination. No evidence of tuberculosis was revealed by any of these sections.

Method 4. Three patients (Nos. 45, 46, and 47), of whom two were in stage III and one in stage II of the disease, were each injected with 0.2 milligram of Koch's therapeutic tuberculin. Seven hours later 5 c.c. of blood were withrawn from each patient. In order to exclude the possible presence of any protective substances the serum was removed from this blood by centrifugalization and 0.5 per cent. sterile acetic acid added to the blood. The centrifuge tube was then closed with a sterile rubber cork, thoroughly shaken, and centrifuged. The resulting sediment was injected intraperitoneally into a guinea-pig. These three pigs were chloroformed seventy-four days after inoculation. Careful autopsies were performed and material taken from the various organs for microscopic examination. Of these three inoculations one (Case 45) yielded a positive result and extensive tuberculosis of the lungs, liver, spleen, and lymph glands were found.[38]

Method 5. From each of five far-advanced cases 5 c.c. of blood were withdrawn, centrifuged, and the supernatant serum removed. The sediment was then treated with 0.5 per cent. sterile acetic acid and centrifuged. The resulting sediment was implanted upon ten culture tubes of gential violet. No growth was obtained at the end of two weeks, on any of the tubes.[39]

SUMMARY. A number of different methods have been employed by us to determine whether tubercle bacilli are present in the circulation of patients with advanced pulmonary tuberculosis.

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[37] Ueber das Vorkommen von Tuberkelbacillen im Strömenden Blut beim tuberkulosen u. tuberkulinsierten meerschweinschen, Beitr. z. klin. d. Tuberk., 1914, xxxi, Hft. 1, 71.

[38] Further experiments along these lines are now in progress and will be the subject of a later report.

[39] I am indebted to Mr. Pertroff, of the laboratory at the Adirondack Cottage Sanitarium, for giving me the gentian-violet media.

1. Blood withdrawn from thirty-eight patients was inoculated intraperitoneally into guinea-pigs. Autopsies and microscopic sections two to three months later failed to reveal any evidence of tuberculosis.

2. Microscopic examination of the blood withdrawn from ten patients yielded negative results. The many sources of error in the microscopic examination of blood for tubercle bacilli have been pointed out.

3. The blood of seven patients previously subjected to a tuberculin injection was inoculated intraperitoneally into guinea-pigs. Autopsies and microscopic sections failed to reveal any evidence of tuberculosis.

4. In three patients who had previously received a tuberculin injection, blood was withdrawn and after removal of the serum was inoculated intraperitoneally into guinea-pigs. One of the pigs developed an extensive tuberculosis.

5. An attempt made to grow the tubercle bacilli directly from the blood proved unsuccessful.

Discussion. The negative results yielded by these forty-seven cases do not prove conclusively that tubercle bacilli are never present in the circulation, but they strongly suggest that a bacillemia such as is present in other infectious diseases is at least uncommon in pulmonary tuberculosis even in advanced stages of the disease. It may be that from time to time tubercle bacilli are washed into the circulation from a pulmonary focus, and that they rapidly disappear from the blood. That such a rapid departure from the blood does occur, has been demonstrtaed in the case of rabbits in whom tubercle bacilli could no longer be recovered from the blood thirty minutes after their intravenous inoculation (Heymann and Otto).[40]

When the blood of ten patients previously subjected to a tuberculin injection was inoculated into guinea-pigs, one of the animals presented a generalized tuberculosis at autopsy. It would be unwise to draw conclusions from one positive result, but the nine negative results coincide with our daily clinical experience, for if a therapeutic tuberculin injection could cause virulent tubercle bacilli to appear in the circulation the development of acute miliary tuberculosis would be a common occurrence. Nevertheless, the question of a possible mobilization of tubercle bacilli following diagnostic and therapeutic tuberculin inoculations deserves careful investigation.

I wish to take this opportunity to express thanks to the house staff and Dr. Felberbaum of the laboratory for willing aid in carrying out this work.

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[40] Centralbl. f. bacterial Ref., 1913, lvii, 293.

CASE REPORTS.

Case 1.—Stage II. Temperature ranged between 98.6° and 101.4° F. March 27, 1914: temperature, 100.4° F.; 5 c.c. of blood injected into guinea-pig No. 74.

The pig was chloroformed July 21, 1914, one hundred and sixteen days following inoculation. No gross evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal glands; microscopically, no evidence of tuberculosis.

Case 2.—Stage III. Temperature ranged between 96° and 102.4° F. March 31, 1914: temperature, 99° F.; 5 c.c. of blood injected into guinea-pig No. 2.

The pig was chloroformed August 7, 1914, one hundred and twenty-nine days after inoculation. No macroscopic evidences of tuberculosis; retroperitoneal and mesenteric glands were not enlarged; microscopically no evidences of tuberculosis.

Case 3.—Stage III. Temperature ranged between 98° and 104° F. April 7, 1914: temperature, 103.6° F.; 5 c.c. of blood injected into guinea-pig No. 18.

The pig was chloroformed July 24, 1914, one hundred and one days after inoculation. No macroscopic evidences of tuberculosis; microscopically all of the organs appear normal; no enlargement of mesenteric or retroperitoneal glands.

Case 4.—Stage III. Temperature ranged between 97.6° to 103.4° F. April 10, 1914: temperature, 100.4° F.; 5 c.c. of blood injected into guinea-pig No. 11.

The pig was chloroformed August 7, 1914, one hundred and nineteen days after inoculation. There were a number of adhesions between the stomach and liver; no evidences of tuberculosis, either grossly or microscopically.

Case 5.—Stage I. Temperature ranged between 98.2° and 101° F. April 24, 1914: temperature, 100.2° F.; 3 c.c. of blood injected into guinea-pig No. 4.

The pig was chloroformed August 7, 1914, one hundred and five days after inoculation. There are marked adhesions between the spleen and the stomach, also a few adhesions between the parietal peritoneum and intestines; no enlargement of mesenteric or retroperitoneal glands; no gross or microscopic evidences of tuberculosis in any organ.

Case 6.—Stage II. Temperature ranged between 98.8° and 100.4° F. April 24, 1914: 5 c.c. of blood injected into guinea-pig No. 5.

The pig was chloroformed August 7, 1914, one hundred and five days after inoculation. No evidences of tuberculosis, either grossly or microscopically; no enlargement of mesenteric or retroperitoneal glands.

Case 7.—Stage III. Temperature ranged between 98° and 101° F. April 28, 1914: 5 c.c. of blood injected into guinea-pig No. 6.

The pig died June 25, 1914, fifty-eight days following inoculation. No evidence of tuberculosis in any organ, either grossly or microscopically; retroperitoneal or mesenteric glands were not enlarged.

Case 8.—Stage III. Temperature ranged between 97° and 103° F. April 28, 1914: temperature, 100.2° F.; 5 c.c. of blood injected into guinea-pig No. 9.

The pig was chloroformed August 7, 1914, one hundred and one days after inoculation. No evidence of tuberculosis in any organ, either grossly or microscopically; congestion of spleen.

Case 9.—Stage III. Temperature ranged between 97° and 99.2° F. April 28, 1914: temperature, 98.6° F.; 5 c.c. of blood injected into guinea-pig No. 8.

The pig was chloroformed August 7, 1914, one hundred and one days after inoculation. No evidence of tuberculosis in any organ, either grossly or microscopically; no enlargement of mesenteric or retroperitoneal lymph glands.

Case 10.—Stage III. Temperature ranged between 98° and 100° F. April 28, 1914: temperature, 98.8° F.; 5 c.c. of blood injected into guinea-pig No. 7.

The pig was chloroformed August 7, 1914, one hundred and ninety-one days after inoculation. Some adhesive peritonitis present between liver, stomach, and intestines; moderate perisplenitis; no enlargement of mesenteric or retroperitoneal glands. Microscopically all organs negative for tuberculosis.

Case 11.—Stage III. Temperature ranged between 97° and 101° F. May 5, 1914: temperature, 100.4° F.; 5 c.c. of blood injected into guinea-pig No. 12.

The pig was chloroformed August 7, 1914, ninety-four days after inoculation. No evidence of tuberculosis in any organ either grossly or microscopically; mesenteric and retroperitoneal glands not enlarged.

Case 12.—Stage II. Temperature ranged between 98.4° and 102° F. May 5, 1914: temperature, 100.4° F.; 5 c.c. of blood injected into guinea-pig No. 10.

The pig was chloroformed August 7, 1914, ninety-four days after inoculation. Congestion of lungs, otherwise organs negative; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically no evidences of tuberculosis.

Case 13.—Stage III. Temperature ranged between 98° and 101.4° F. May 5, 1914: temperature, 99.4° F.; 5 c.c. of blood injected into guinea-pig No. 11.

The pig was chloroformed August 7, 1914, ninety-four days after inoculation. No gross changes found; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically no evidence of tuberculosis.

Case 14.—Stage II.—Temperature ranged between 98° and 101° F. May 5, 1914: 5 c.c. of blood injected into guinea-pig No. 85.

The pig was chloroformed August 11, 1914, ninety-eight days after inoculation. Spleen somewhat enlarged, otherwise organs appear normal; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically no evidences of tuberculosis in any organ.

Case 15.—Stage III. Temperature ranged between 97.8° and 100° F. May 6, 1914: temperature, 99.6° F.; 5 c.c. of blood injected into guinea-pig No. 56.

The pig was chloroformed August 11, 1914, ninety-seven days after inoculation. No gross or microscopic evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal glands.

Case 16.—Stage II. Temperature ranged between 97° and 101.4° F. May 6, 1914: temperature, 98.2° F.; 5 c.c. of blood injected into guinea-pig No. 15.

The pig was chloroformed August 11, 1914, ninety-seven days after inoculation. Spleen not enlarged, a grayish nodule on the surface microscopically shown to be inflammatory in character, other organs negative for tuberculosis, grossly and microscopically; no enlargement of peritoneal lymph glands.

Case 17.—Stage II. Temperature ranged between 98° and 100.2° F. May 6, 1914: temperature, 99° F.; 5 c.c. of blood injected into guinea-pig No. 16.

The pig died July 28, 1914, eighty-three days after inoculation. Extensive ulceration of back. No evidence of tuberculosis upon gross or microscopic examination; no enlargement of mesenteric or retroperitoneal lymph glands.

Case 18.—Stage III. Temperature ranged between 97° and 101.2° F. May 6, 1914: temperature, 100° F.; 5 c.c. of blood injected into guinea-pig No. 17.

The pig was chloroformed August 11, 1914, ninety-seven days after inoculation. No evidence of tuberculosis upon gross or microscopic examination; no enlargement of mesenteric or retroperitoneal lymph glands.

Case 19.—Stage III. Temperature ranged between 97.2° and 102° F. June 5, 1914: temperature, 100.2° F.; 5 c.c. of blood injected into guinea-pig No. 58.

The pig was chloroformed August 11, 1914, sixty-seven days after inoculation. No gross or microscopic evidence of tuberculosis in any organ; no enlargement of mesenteric or retroperitoneal lymph glands.

Case 20.—Stage III. Temperature ranged between 97.4° and 102° F. June 6, 1914: temperature, 101° F.; 5 c.c. of blood injected into guinea-pig No. 57.

The pig was chloroformed August 11, 1914, sixty-six days after inoculation. No evidence of tuberculosis upon gross or microscopic examination; no enlargement of mesenteric or retroperitoneal glands.

Case 21.—Stage III. Temperature ranged between 97° and 103.8° F. June 8, 1914: temperature, 100° F.; 5 c.c. of blood injected into guinea-pig No. 59.

The pig was chloroformed August 11, 1914, sixty-four days after inoculation. The spleen is very small and is adherent to stomach; no gross or microscopic evidence of tuberculosis; no enlargement of retroperitoneal or mesenteric glands.

Case 22.—Stage III. Temperature ranged between 97° and 102.4° F. June 8, 1914: temperature, 100.4° F.; 5 c.c. of blood injected into guinea-pig No. 84.

The pig was chloroformed August 11, 1914, sixty-four days after inoculation. No gross or microscopic evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands.

Case 23.—Stage III. Temperature ranged between 97° and 100.8° F. June 9, 1914: temperature, 100.2° F.; 5 c.c. of blood injected into guinea-pig No. 61.

The pig died August 14, 1914, three days after delivery; sixty-six days after injection. Congestion of lungs, purulent peritonitis, cloudy swelling of viscera; no evidence of tuberculosis in any organ; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopic examination negative for tuberculosis.

Case 24.—Stage III. Temperature ranged between 97.4° and 100.6° F. June 9, 1914: temperature, 98° F.; 5 c.c. of blood injected into guinea-pig No. 62.

The pig was chloroformed August 11, 1914, sixty-three days after inoculation. Spleen slightly enlarged; no evidence of tuberculosis in any organ upon microscopic examination; no enlargement of mesenteric or retroperitoneal lymph glands.

Case 25.—Stage III. Temperature ranged between 98° and 101° F. June 9, 1914: temperature, 99.6° F.; 5 c.c. of blood injected into guinea-pig No. 64.

The pig was chloroformed August 15, 1914, sixty-seven days after inoculation. Spleen very much enlarged, weighs 5 grams; no gross evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically organs appear normal.

Case 26.—Stage III. Temperature ranged between 98° and 102.4° F. June 9, 1914: temperature, 100.2 F.; 5 c.c. of blood injected into guinea-pig No. 65.

The pig died July 26, 1914, forty-seven days after inoculation. Purulent pericarditis; purulent inflammation of left lung; pneumonia in right lung; cloudy swelling of other viscera. Microscopically no evidence of tuberculosis.

Case 27.—Stage III. Temperature ranged between 97.6° and 100.6° F. June 10, 1914: 5 c.c. of blood injected into guinea-pig No. 66.

The pig was chloroformed August 15, 1914, sixty-six days after inoculation. No gross or microscopic evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands.

Case 28.—Stage III. Temperature ranged between 97.6° and 102° F. June 9, 1914: temperature, 99.6° F.; 5 c.c. of blood injected into guinea-pig No. 67.

The pig died July 26, 1914, forty-seven days after inoculation. Patches of bronchopneumonia in left lung; purulent peritonitis; cloudy swelling of liver, spleen, and kidneys. Microscopically no evidences of tuberculosis.

Case 29.—Stage III. Temperature ranged between 97° and 102° F. June 9, 1914: temperature, 100° F.; 5 c.c. of blood injected into guinea-pig No. 68.

August 15, 1914, sixty-seven days after inoculation, the pig was etherized. No evidence of tuberculosis upon gross examination. Microscopically the organs were normal.

Case 30.—Stage III. Temperature ranged between 98° and 102.8° F. June 10, 1914: temperature, 100.8° F.; 5 c.c. of blood injected into guinea-pig No. 63.

The pig was etherized August 15, 1914, sixty-six days after inoculation. Few peritoneal adhesions, no glandular enlargement. Microscopically no evidence of tuberculosis.

Case 31.—Stage III. Temperature ranged between 97.4° and 102° F. June 11, 1914: temperature, 99.4° F., 5 c.c. of blood injected into guinea-pig No. 69.

The pig was etherized August 15, 1914, sixty-five days after inoculation. No gross or microscopic evidence of tuberculosis; no enlargement of retroperitoneal or mesenteric lymph glands.

Case 32.—Stage III. Temperature ranged between 97° and 102.4° F. June 11, 1914: temperature, 101° F.; 5 c.c. of blood injected into guinea-pig No. 70.

The pig was etherized August 15, 1914, sixty-five days after inoculation. No gross or microscopic evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands.

Case 33.—Stage III. Temperature ranged between 97° and 103.6° F. June 12, 1914: temperature 102° F.; 5 c.c. of blood injected into guinea-pig No. 71.

The pig died August 8, 1914, fifty-seven days after inoculation. Small cyst at lower pole of right kidney, otherwise negative; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically, negative.

Case 34.—Stage III. Temperature ranged between 97.4° and 102° F. June 12, 1914: temperature, 99.4° F.; 5 c.c. of blood injected into guinea-pig No. 72.

August 15, 1914, the pig was etherized, sixty-four days after inoculation. No gross or microscopic evidence of tuberculosis.

Case 35.—Stage II. Temperature ranged between 97° and 100° F. June 12, 1914: temperature, 98.8° F.; 5 c.c. of blood injected into guinea-pig No. 73.

August 15, 1914, the pig was etherized, sixty-four days after inoculation. No gross evidence of tuberculosis. Microscopically the organs were normal.

Case 36.—Stage II. Temperature ranged between 97° and 101.6° F. June 19, 1914: Koch's therapeutic tuberculin 0.1 mgm. injected at 9 a.m. Temperature, 100.2° F.; 4.5 c.c. of blood injected into guinea-pig No. 75 at 4 p.m.

The pig was chloroformed September 18, 1914, ninety-one days after inoculation. No evidence of tuberculosis; mesenteric and retroperitoneal glands are not enlarged. Microscopically negative for tuberculosis.

Case 37.—Stage III. Temperature ranged between 97° and 100° F. June 19, 1914: Koch's therapeutic tuberculin 0.1 mgm. injected at 9 a.m. Temperature, 99.2° F.; 2.5 c.c. of blood injected into guinea-pig No. 76 at 4 p.m.

The pig was chloroformed September 18, 1914, ninety-one days after inoculation. No evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically all the organs were normal.

Case 38.—Stage III. Temperature ranged between 97° and 100° F. June 19, 1914: Koch's therapeutic tuberculin 0.1 mgm. injected at 9 a.m. Temperature, 99.2° F.; 5 c.c. of blood injected into guinea-pig No. 77 at 4 p.m.

The pig was chloroformed September 18, 1914, ninety-one days after inoculation. A few adhesions found between intestine and liver; spleen embedded in a mass of adhesions. Microscopically negative for tuberculosis.

Case 39.—Stage III. Temperature ranged between 97° and 100.4° F. June 23, 1914: Koch's therapeutic tuberculin 0.2 mgm. injected at 9 a.m. Temperature, 100.4° F.; 5 c.c. of blood injected into guinea-pig No. 81 at 4 p.m.

The pig was chloroformed September 18, 1914, eighty-seven days after inoculation. No gross evidences of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically organs are negative.

Case 40.—Stage II. Temperature ranged between 98° and 101.8° F. July 7, 1914: Koch's therapeutic tuberculin 0.2 mgm. injected at 9 a.m. Temperature, 101° F.; 5 c.c. of blood injected into guinea-pig No. 78 at 4 p.m.

The pig was chloroformed September 18, 1914, seventy-three days after inoculation. No gross evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically all the organs are negative.

Case 41.—Stage III. Temperature ranged between 98° and 100.4° F. July 13, 1914: Koch's therapeutic tuberculin 0.2 mg. injected at 9 A.M.; 5 c.c. of blood injected into guinea-pig No. 79 at 4 P.M.

The pig died August 20, 1914, thirty-eight days after inoculation. No gross evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically all the organs are negative.

Case 42.—Stage III. Temperature ranged between 98° and 100.6° F. July 13, 1914: Koch's therapeutic tuberculin 0.1 mg. injected at 9 A.M. Temperature, 99.6° F.; 5 c.c. of blood injected into guinea-pig No. 82 at 4 P.M.

The pig was chloroformed September 18, 1914, sixty-seven days after inoculation. No gross evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically all the organs are negative.

Case 43.—Stage III. Temperature ranged between 98° and 104° F. July 21, 1914: temperature, 103° F.; 2.5 c.c. of blood injected into guinea-pig No. 83.

The pig was chloroformed September 18, 1914, fifty-nine days following inoculation. No gross evidence of tuberculosis; no glandular enlargement. Microscopically all the organs are negative.

Case 44.—Stage III. Temperature ranged between 97° and 102° F. July 28, 1914: temperature, 99.2° F.; 4 c.c. of blood injected into guinea-pig No. 86.

October 13, 1914, seventy-seven days following inoculation, the pig was chloroformed; no microscopic evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically the organs are negative.

Case 45.—Stage II. August 1, 1914, 0.2 mg. of Koch's therapeutic tuberculin injected at 9 A.M. Temperature, 100.4° F.; seven hours after injection of tuberculin, 5 c.c. of blood withdrawn. Blood treated as described in text. Sediment injected into guinea-pig No. 89.

October 13, 1914 the pig was chloroformed, seventy-four days following inoculation. Tuberculosis of lungs, liver, spleen, and lymph glands. December 8: no apparent change in clinical condition of patient. No temperature changes followed above experiment.

Case 46.—Stage III. Temperature ranged between 97° and 101.6° F. August 1, 1914, seven hours after injection of 0.2 mg. of Koch's therapeutic tuberculin, temperature, 99.4° F.; 5 c.c. of blood injected into guinea-pig No. 88. Blood treated as in Case 45.

The pig was chloroformed October 13, 1914, seventy-four days after inoculation. No gross evidence of tuberculosis. Microscopically all organs are negative.

Case 47.—Stage III. Temperature ranged between 99° and 100.4° F. August 1, 1914, seven hours after inoculation with 0.2 mg. of Koch's therapeutic tuberculin, 5 c.c. of blood taken from patient and injected into guinea-pig No. 90. Blood treated as in Cases 45 and 46.

The pig was chloroformed October 13, 1914, seventy-four days after inoculation. No macroscopic evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically all the organs are negative.

Case 48.—Stage III. Temperature ranged between 97° and 102.4° F. June 8, 1914: temperature, 100.4° F.; 5 c.c. of blood injected into guinea-pig No. 60.

The pig was chloroformed September 18, 1914, one hundred and two days after inoculation. No gross evidence of tuberculosis; no enlargement of mesenteric or retroperitoneal lymph glands. Microscopically no evidence of tuberculosis found.

PRURIGO NODULARIS AND LICHENIFICATION WITH TUMOR FORMATION.

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One of the cases about to be described is from the service of Dr. Trimble, at the University and Bellevue Dermatological Clinic, and to him I am indebted for the privilege of recording it; the other is from the out-patient department of the Roosevelt Hospital. The case histories follow:

Case I.—Mr. G. S., aged seventy-three years, a shoemaker, born in Germany. For the past eleven years he has suffered from moderate dyspnea on exertion, and he often has a cough in the early winter, but this is not serious. His bowels are regular, but sweet food is apt to start a mild diarrhea. He seldom suffers from headache. His general health was good until the spring of 1910, when he was taken sick rather suddenly with increased frequency of micturition, pain across the back, especially on the left side, which was tender to the touch, and stiffness of the muscles of the back. He was in bed for five weeks, and was told that he had kidney and stomach disease. There has been no return of these symptoms, but he has never been as well since, and is sleepy and tired most of the time.

Itching of the skin began immediately after this attack, and was and is generalized. Papules have been present from the start, and at no time has the skin been free of the eruption; indeed, the patient cannot be sure of any period of improvement. There has never been any exudation, although the skin is often scratched until blood flows.

The eruption involves the greater part of the trunk and extremities. On the back it extends over the whole lumbar region, with an extension upward on the right to the middle of the shoulder blade, and on the left, along the posterior axillary fold, nearly to the axilla. These upward extensions show only a slight drying and thickening of the skin, with a few scratched papules and slight pigmentation.

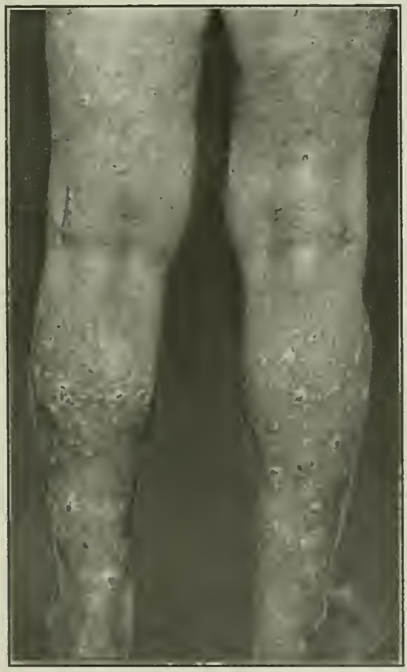

FIG. I.—Lichenification with tumor formation. Mr. G. S.

The skin over the pubes is dry and thick, the process extending along the linea alba to the navel. The skin in the folds of the groin is thickened and purplish.

The lower extremities are affected in their entirety, except for the upper antero-internal surface of the thighs, an area about three inches in diameter over each trochanter, and the soles of the feet.

The upper extremities are less involved, the eruption being confined to the external and the posterior radial surfaces of the forearms.

The affected surface is dry and harsh. The smallest lesions are only slight exaggerations of the normal cross-hatching of the skin. Next come small papules, which seem to be thickenings of the deeper layers of the skin, the horny layer being but little affected. The smallest lesions are shiny and flat-topped; the next larger ones are rounded and not particularly shiny. The color of the earliest lesions and of those of the second class also is that of the normal skin, except that in patches of long standing their color is that of the surrounding skin—a dull purple. The larger papular lesions are all scratched, as are also most of the others. Some of the papules seem to be receding; on the forearms are many white spots of thickened skin, which appear to be the remains of former lesions. The greatest thickening and the greatest number of papules occur on the lower legs, where the eruption first developed. The forearms show no large papules, and few occur on the back. The general effect is one of extending and increasing lichenification, with firm papules or nodules arising from the middle of the lichenified areas. The nodules appear to be localized exaggerations of a general process rather than a separate condition.

No urticarial or erythematous lesions were observed. Treatment was practically without effect.

Case II.—Miss S. O., a Swede, aged twenty-five years, employed in the linen room of a New York hotel, applied for treatment at the out-patient department of Roosevelt Hospital in December, 1913. There is no tuberculosis in her family and no skin disease like hers. Her father is alive at sixty-three, and is alcoholic; her mother is about fifty-five years old, and healthy. The patient states that she has had measles and whooping cough, but not scarlet fever. She has always been constipated. She says that she had chills and fever every day for two years until she was seventeen years old. She has never been subject to hives. Her hair has always been thin, and her skin coarse and harsh, but it does not chap severely. On the other hand, her skin blisters easily from moderate heat, and develops callosities rather readily. She states that in August, 1911, a papule appeared on her left forearm, perhaps from an insect bite; this she scratched. Two weeks later a boil developed at the site of the original papule, and from that time until the end of the year a series of boils occurred on both forearms. During this time she noticed that on coming into a warm room from the cold air outside there appeared on the hand and ankles a number of small firm nodules, which burned and itched badly. The color was that of the normal skin or a little darker, but not red.

She was admitted to the New York Skin and Cancer Hospital in November, 1911, her hands being then so badly crippled by boils that she could hardly use them. She remained in the hospital about four months, and in that time the boils were healed and have not returned, but the nodules were unchanged.

New nodules have appeared from time to time, the eruption gradually creeping up the extremities toward the trunk. The patient states that after severe scratching and removing the thickened, horny layer, which brings with it a horny plug or kernel, the itching subsides and the papules flatten down to a slight thickening in the skin, but that they never disappear entirely, and increase in size again when irritated. She states that irritation of an old flattened lesion will often produce a blister containing bloody serum. She insists that the papules appear first and increase under scratching, but that scratching of healthy skin is not followed by the development of a papule. The itching, which appears to be limited to the lesions, is very severe, and often interferes with sleep. It is worse whenever the patient is more than usually nervous and whenever her mind is not distracted by her occupation. It is also worse the first day or two of the menses, but there is no increase in the size of the lesions at that time.

For the past year or two the patient has often been sleepy in the afternoon, and her legs have ached badly after slight exertion, like going up stairs. Headaches were infrequent until the summer of 1913, since which time they have been quite common; and more recently she has been subject to attacks of overpowering sleepiness, lasting ten to fifteen minutes, and then passing off suddenly. All these constitutional symptoms are relieved or removed by careful attention to the bowels.

When examined by me, December 16, 1913, the skin of the face was rough, coarse, and muddy looking, but no distinct tumors were made out. The tongue showed upon the right side of the dorsal surface a white sclerotic area dotted with a few red spots, about a quarter of an inch broad and an inch long, the anterior extremity being about three-quarters of an inch from the tip of the tongue. This area is depressed slightly below the level of the adjoining mucous membrane, but is not ulcerated. The patient says that it has grown from a spot about the size of a pea in the past year or less. A later examination revealed a firm white nodule about a quarter of an inch in diameter on the right side of the bottom of the tongue just below this white plaque. It was not so hard as to suggest cancer, and gave one the impression that it was produced by the same process which had caused the tumors in the skin.

The characteristic nodules were scattered over both upper and lower extremities. There was no tendency to grouping, and flexor and extensor surfaces were involved alike. Two papules were found on the left thenar eminence, and one on the right palm; otherwise the palms were free. Forty-four lesions of all sizes were counted on the back of the right hand and fingers, and fifty-five on the left, and they were almost as thickly scattered over both forearms and legs. There were a few papules on the arms and one small one on the left side of the neck. On the back of the neck, about an inch to the right of the middle line and just below the hair, there was a papule about three-sixteenths of an inch in diameter, exactly like the others, which is said to have appeared after the removal of a growth of unknown nature from the same spot eight or nine years ago. The earliest lesions appeared to be small nodules in or under the skin, the epithelium above them unchanged. In the older lesions the epithelium was thickened, pink or light brownish in color, and generally slightly rough and warty, but without any papillary projection or deep depressions. The lesions on the upper part of the arms, where the disease seemed to be spreading, were, as a rule, small, about one-eighth of an inch in diameter, and showed but little elevation. Some were scarcely perceptible, while the largest tumors on the hands were three-eighths of an inch in diameter, and on the legs, seven-sixteenths of an inch. Many of the medium-sized and large lesions were capped by a brownish crust. The removal of the thickened epithelium from the medium-sized tumors revealed a shallow crater, the concavity of which was studded with many fine bleeding points. Crusts removed from the tops of some of the older lesions showed filiform horny plugs about a sixteenth of an inch long projecting from the under surface.

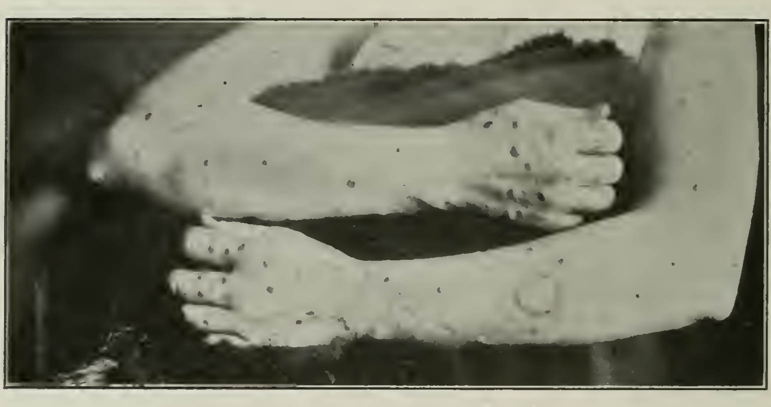

FIG. 2.—Prurigo nodularis. Miss S. O.

An area on the forearm, about an inch and a half in diameter, entirely free of the eruption, was enclosed in a line drawn with silver nitrate. The reaction to the caustic was unusually severe. A painful blister formed where the line had been, and when this ruptured and dried, a red line was left, which remained for weeks. The patient was instructed to scratch this enclosed area repeatedly, and this she assures me she has done, but no sign of tumor formation has appeared.

The Wassermann reaction and the Morro tuberculin reaction were both negative.

On February 6, 1914, the patient came to me to show a group of ecchymoses, covering an area about two inches by four inches, on the inner aspect of the right knee, extending up a little on to the thigh. The largest spot was of irregular outline, about one inch by two; the others were rounded, about a quarter of an inch to an inch in diameter. They were of a dull purple color. There were similar patches on the left instep. They were said to have appeared February 4, and the patient states that similar lesions have occurred at intervals for the past six months, each outbreak lasting a week or two. They seem to have no connection with menstruation, constipation, or errors of diet, but are usually preceded and accompanied by a period of intense itching. At the outbreak of this attack the patient was on a low protein diet, eating meat but once a week, and nevertheless complaining of aching of the muscles on slight exertion.

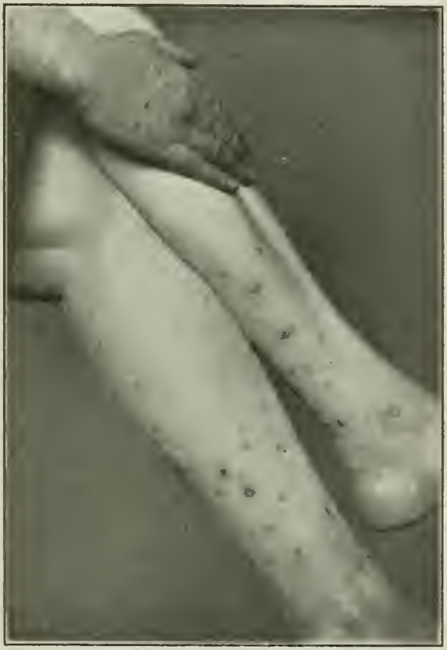

FIG. 3.—Prurigo nodularis. Miss S. O.

On this date a group of four small papules was discovered, forming a line about an inch long, the lowest one about an inch and a half above the inner end of the right clavicle. They were said to have been present for several months, at times hardly visible, but very prominent at periods of increased itching.

On February 18, three white spots, each about three-quarters of an inch in diameter, appeared on the back. They were very itchy, and the surrounding skin was red. They lasted not over two days.

Nodules were excised from the right arm on December 16, 1913, for microscopic examination. The wounds healed readily, but within a few weeks a fresh nodule had developed at the site of one of those excised. It is to be noted also that a nodule is present in the scar left by a biopsy performed at the Skin and Cancer Hospital. Another nodule was removed from the leg on March 11, 1914. The microscopic examination of these nodules revealed no features not already described by previous authors.

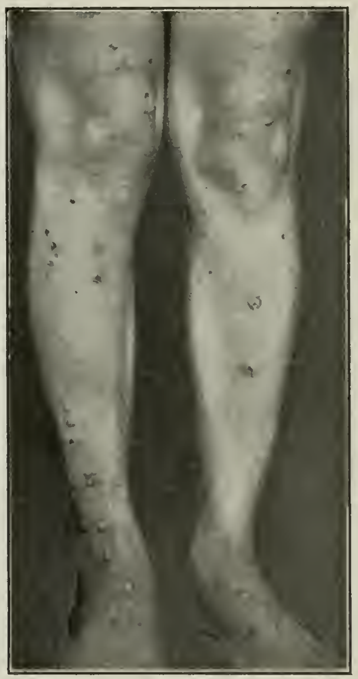

FIG. 4.—Prurigo nodularis. Miss S. O.

DISCUSSION. The two cases present many points of similarity, and yet differ in several very important respects. In both there is intense itching, long duration, and the appearance of firm papules. Both patients state that papules have been present from the start, but a careful examination of the man shows broad areas of skin where lichenification is in progress, with no well-defined papules at all, or only doubtful ones in the older parts. It is only on the legs, where the disease began, that large papules are found, and wherever there are well-marked papules the skin between is pigmented, markedly thickened, and shows many white, firm scar-like spots, which appear to mark the sites of former papules. The appearance of the woman's skin is entirely different. In her case the tumors arise from an apparently normal skin, and in the places where the disease has most recently appeared, as on the arms, there is no sign of thickening or lichenification, but, on the other hand, distinct, though small, papules. The same holds true of her hands and ankles, where the disease first appeared; the skin is coarse and harsh, it is true, but only slightly thickened and not lichenified. She insists that a tumor, once established, never disappears entirely, and her statement is borne out by the appearance of the skin and its behavior during the four months it has been under observation.

These two patients may be taken as examples of two distinct clinical conditions, a number of examples of each of which have been recorded in medical literature. The group represented by the woman includes cases reported by Hardaway,[1] Baker,[2] Johnson,[3] Kreibich,[4] Hjelmann,[5] W. Pick,[6] Brocq,[7] Schamberg and Herschler,[8] C. J. White,[9] Hyde,[10] Jackson,[11] Fasal,[12] Zeisler,[13] Sutton,[14] and Stelwagon.[15]

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[1] Case of Multiple Tumors of the Skin, Accompanied by Intense Pruritus, Arch. Dermat., 1880, p. 129.

[2] Cited by Crocker, Trans. Internat. Med. Cong. at Rome 1894, p. 34, and Dis. of Skin, 3d ed., Phila., 1908, i, 162.

[3] A Papular Persistent Dermatosis, Jour. Cut. Dis, 1899, p. 49 (with illustrations).

[4] Ueber Urticaria Chronica (Two Cases Described as Urticaria Perstans Verrucosa), Arch. f. Dermat. u. Syph., 1899, xlviii, 163 (with illustration).

[5] Ett fall af urticaria perstans verrucosa, Finska Läkaresällskapets Handlingar, 1899, xli, 1236 (with illustrations). An abstract of this report is printed in the Jour. Cut. Dis., 1900, p. 470, and is probably the source of information of most authors who refer to the case. It is credited to the St. Louis Med. and Surg. Jour., where an article with a similar title appears on page 96, published August, 1900. This article is itself an abstract, and is credited to Bull. Med. and Surg., 1900. There was no such periodical as Bulletin of Medicine and Surgery in the year 1900, but the Medical Bulletin of Philadelphia, May, 1900, p. 175, contained an article almost identical with those mentioned above, which it ascribes to Prog. Med., but without mentioning date or page. This might refer to Progressive Medicine, but it does not; the article is a translation of an abstract in Le Progrès Médical, January 27, 1900, p. 60. The French journal gives no hint of the source of its abstract.

[6] Ein Fall von sogennanter Urticaria perstans, Stereoscop. Med. Atlas, 40, Lieferung, Dermatologie, 15 Folge. A. Neisser. Tafel 475. 1901.

[7] Lichen obtusus corné (five cases), La Prat. Dermat., 1902, iii, 201 (with illustrations).

[8] Two Cases of Multiple Tumors of the Skin in Negroes Associated with Itching, Jour. Cut. Dis., 1906, p. 151 (with illustrations).

[9] Lichen Obtusus Corneus, Jour. Cut. Dis., 1907, p. 386.

[10] Prurigo Nodularis, Diseases of the Skin, Phila., 1909, p. 174.

[11] Case of Multiple Tumors Associated with Itching, Jour. Cut. Dis., 1909, p. 39.

[12] Arch. f. Dermat. u. Syph., 1912, cxii, 265.

[13] A Case of So-called Prurigo Nodularis, Jour. Cut. Dis., 1912, p. 654 (with illustration).

[14] A Differential Study of Prurigo Nodularis and Urticaria Perstans, Arch. Diagnosis, 1913, p. 341 (with illustrations), also Jour. Amer. Med. Assoc., January 17, 1914, p. 181.

[15] Diseases of the Skin, 7th ed., Phila., 1914, p. 212.

These cases form a well-defined group, with many points of resemblance, and few of difference. The illustrations are strikingly alike, and often those published for one case would serve as well for another. The essential features are:

1. An eruption of firm, round or oval tumors, beginning as scarcely perceptible papules, and reaching a size of half an inch in diameter. They form rounded elevations, becoming flat-topped in the later stages, or even slightly depressed in the center. The early lesions are smooth, the older ones rough and warty. Color is not a distinctive feature—it may be that of normal skin, or pinkish, or brown, or yellowish, or gray.
2. A lesion, once well developed, seldom or never entirely disappears.
3. Itching is intense, and always accompanies or follows the development of a papule, and does not precede it.
4. The skin between the lesions is approximately normal.

Taking up in order these features of the disease, it is to be noted that the descriptions given by the observers are singularly uniform. There is some slight variation in the color and size of the lesions observed, but the color is never a marked feature, and the size varies in individual cases.

The persistence of the individual lesions has been noted by all the observers. In only four of the cases is it recorded that any of the growths have disappeared, and then only a few, while in seven it is distinctly stated that a lesion once established never disappears, and in four others it is noted that there was no change save in the size of the tumors. Of the remaining seven, one was under observation a few days only, in which time no change was observed, one showed infiltrated pigmented spots corresponding to involuted lesions, and five are those recorded by Brocq, who gives no detailed histories, but who states that the evolution is very slow. Recurrence after excision is reported in six of the cases, a high percentage, when we consider that in only nine of the cases are the histories complete enough or the period of observation long enough to judge of this feature.

The itching is a very prominent feature and was exceedingly severe in all cases, so severe as to prevent sleep, and to interfere with the daily occupation. It seems to be a symptom of the eruption, and not the cause of it. This is expressly so stated in Johnston's case and my own. Hardaway's patient, it is true, stated that each tumor arose at an itching point as a result of scratching, but Hardaway expressly states that he was unable to confirm this. I may add that repeated scratching on a small area of the forearm in my own patient was followed by no change in the skin whatever. The usual report is that the disease began as papules with itching. In five cases the itching is said to be limited to the lesions themselves, and in two cases to the lesions and their immediate neighborhood.

The skin between the lesions is normal or nearly so. The only exceptions to this rule are Hardaway's case, in which the disease had been present for twenty-two years, and in which the skin was coarse, rough, pigmented, and much thickened, and Johnston's, where the disease was of ten years' duration, in which there was some lichenification on the forearms and legs, but none on the face. Johnston remarks that this was the result of scratching, and that the pruritus which led to the scratching invariably accompanied the growth of a nodule and never preceded it.

In the case here recorded the itching was made worse by constipation and by overeating, but although the symptoms of intestinal indigestion were relieved by a restricted diet and attention to the bowels, the papules showed no change at all, and itching persisted. It seems probable that some disorder of metabolism is responsible for the disease, but what it is we do not know. The occurrence of attacks of urticaria in several of the patients, and of purpura also in the case here recorded, points strongly to a toxemia.

There are also a number of other cases recorded in German literature, generally under the name of urticaria perstans, which bear a considerable resemblance to this group, but which lack, as a rule, one or two of the essential elements. In many of them the urticarial element predominates, and the lesions, though persisting a few weeks, are not permanent. Hartmann's[16] Case III, more fully described later by Hübner,[17] is the one in which the resemblance is most striking; but here also the lesions do not appear to have been permanent, and in the second place, Hübner states that the tumors were caused by the scratching. This brings us to the second group of cases, of which G. S. may be taken as the type, and to which many of the German cases appear to belong. The distinguishing characteristic of this group is the development of tumors as a result of scratching. As the itching precedes the tumor formation, there is a more or less diffuse thickening and pigmentation of the skin, and from this area the papules arise, run their course, and disappear. There are usually many pigmented or atrophic areas which apparently occupy the sites of former lesions, and which form a rather conspicuous element of the clinical picture. Hartmann's Case IV and Case VI seem to belong to this group, and also Kreibich's case, recorded as urticaria perstans papulosa. As the disease is essentially an unusual reaction of the skin to traumatism, the clinical features are somewhat more varied and do not form so well-defined a symptom-complex as those classed as prurigo nodularis.

Török's[18] report on the changes in the skin produced by mechanical irritation is very enlightening in this respect, as he was able to induce similar changes, though of a much milder grade, by rubbing areas of normal skin day after day; and states that in certain pathological conditions the effects of irritation are much more pronounced.

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[16] Ueber eine urticaria artige Hauterkrankung., Arch. f. Dermat. u. Syph., 1903, lxiv, 381.

[17] Ueber Tuberosis cutis pruriginosa, Arch. f. Dermat. u. Syph., 1906, lxxxi, 209.

[18] Welche Hautveränderungen können durch mechanische Reizung der Haut hervorgerufen werden? Arch. f. Dermat. u. Syph., 1902, lxiii, 39.

My thanks are due to Dr. Trimble for the privilege of recording one of the cases, and for photographs of both of them, and to Dr. M. L. L. Welzmiller, for assistance in preparing the histological material.

A STUDY OF GASTRIC SEDIMENTS AND THEIR INTERPRETATION.

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Several years ago in aspirating the contents of a stomach by means of an Ewald aspirating bulb I noticed on the withdrawal of the tube that a small piece of tissue had been caught in the eye of the tube. This little fragment (although not more than 2 mm. in size), appropriately hardened and stained, gave a beautiful picture of the glandularis and muscularis mucosæ, at which level rupture had taken place. The case was one of gastritis acida, and I was impressed particularly with the desquamation and exfoliation of the cells at the periphery, to which attention has previously been called.[1] Thinking that such desquamation and other degenerative changes might occur more frequently than was generally believed, I determined to make the recovery of gastric sediments a routine procedure.

The first method employed was to save all of the wash water from the lavage of the fasting stomach and allow it to sediment by gravity in 1000 c.c. conical graduates, and after a few hours to decant the supernatant fluid down to the last 100 c.c., and on centrifuging this, lift up the sediment by a platinum loop, and after making an ordinary slide smear, to stain it, differentially, with eosin and methylene blue. Crude though this method was, one was often repaid by recovering recognizable elements, such as leukocytes, moulds, fungi, various bacterial groups, and, surprisingly, often epithelial cells or even bits of mucosa, from a study of which it seemed possible to make certain definite diagnostic inferences. There were marked disadvantages, however, in having to deal with large amounts of lavage water, often 3000 or 4000 c.c., which required several hours to settle before being centrifuged, during which time many regressive degenerative alterations might occur in standing at room temperature. Furthermore, the making of even several platinum loop smears, from the centrifuge sediment, only represented a fractional amount of the total sediment. So after various modifications were applied the following method was adopted and carried out, first in the gastro-intestinal department of the German Hospital and later in the stomach clinic at Jefferson Hospital.

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[1] Cf. Anthony Bassler, Med. Rec., November 30, 1907.

To make the procedure less formidable to the patient, instead of using the ordinary size stomach tube the use of a small metal capsule was suggested by my colleague, Dr. J. Quincy Thomas. This capsule is 1.5 cm. long by 6 mm. in diameter, and having a shaft 4 mm. long by 3 mm. in diameter, to which a small capillary rubber tube is securely fastened by a silk thread. The capsule is perforated at the extreme tip with a hole 1.5 mm. in diameter, in a line continuous with the caliber of the tube, and the body of the capsule is similarly perforated with eight additional holes 1.5 mm. in diameter. To facilitate cleaning the capsule is made in two parts, which unite by a screw thread. These metal tips are similar to those introduced by Einhorn for the recovery of duodenal contents or for duodenal feeding, but are made of German silver and silver plated, which is inexpensive and serviceable. The capillary rubber tube attached to this capsule is 1 meter long and of various calibrations. The smallest one that can be serviceably used is 3 mm. in diameter. This tube can be readily swallowed with minimal discomfort, and can be left *in situ* for several hours to admit of fractional analysis of the gastric juice after an Ewald breakfast, or allowed to pass into the duodenum for the recovery and analysis of duodenal or jejunal contents.

A good routine practice is to have the patient swallow the capsule and tube on an empty stomach, preferably in the early morning fasting state, and by means of a one- or two-ounce aspirating syringe, with a capillary tip and supplied with a close-fitting asbestos plunger, gentle aspiration is made to recover the residual contents of the fasting stomach, after which from 100 to 150 c.c. of plain, warm water is introduced by means of the syringe and gently aspirated and forced back again into the stomach, perhaps a dozen times. After the first several re-aspirations it can be usually observed that the lavage water, which was at first macroscopically clear, becomes gradually turbid and contains variously-sized flocculent bodies, ranging from pin-point to 3 to 5 mm. in size. During this period of aspiration and re-injection a stethoscope should be applied to the abdominal wall in the gastric area, and the size, shape, and position of the stomach can be readily mapped out by determining the maximum lines of intensity of the auscultatory tinkling and bubbling sounds. After thus douching the gastric mucosa, all of the fluid is aspirated from the stomach and then a small portion tested for occult blood and the remainder mixed with equal parts of a 10 per cent. solution of formalin. The residual gastric contents or material aspirated from the stomach is recorded in cubic centimeters, allowed to filter, and the filtrate tested for its acidity to determine hypersecretory states; the filter paper is then punctured and the residue washed into a clean bottle with the 10 per cent. formalin solution, and both specimens, properly labeled, are then sent to the laboratory to be handled in the following way:

TECHNIC OF PREPARING SEDIMENTS FOR STAINING. 1. Add to gastric washings an equal quantity of 10 per cent. formalin and allow to stand for at least three hours.

2. Filter through a smooth filter paper. After filtration wash the sediment down to the tip of the filter paper by means of a wash bottle.

3. Cut off the tip of the filter paper containing the sediment. Fold the paper to prevent the escape of the sediment. Wrap the paper in one layer of gauze; tie it fast with a thread.

4. Place in acetone I for one hour.
5. Place in acetone II for one hour.
6. Place in acetone III for two hours.
7. Place in paraffin and chloroform, each one hour.
8. Place in paraffin (M. P., 52° C.), each one hour.
9. Place in paraffin (M. P., 52° C.), each two hours.
10. Imbed in paraffin.
    - (*a*) Attach to a block of vulcanized fiber by means of melted paraffin a piece of cardboard, 6 x 12 x 2 mm.
    - (*b*) Unfold the filter paper and remove the sediment. Mold it into a small block and attach to the pasteboard with melted paraffin.
    - (*c*) Wrap around the block a piece of paper 25 mm. wide, previously dipped in paraffin.
    - (*d*) Float block in iced water and fill the paper box with melted paraffin (M. P., 52° C.)
    - (*e*) Trim the paraffin down to the plane of sediment.
11. Cut serial sections.

12. Float the sections on warm water and place them on slides previously covered with a thin layer of Meyer's egg albumen.

13. Wipe off the excess of water from the edges of the slides.

14. Place the sections in a dry heat sterilizer, at 70° to 80° C., for thirty minutes or until sections are perfectly dry.

Staining. 15. Place sections in xylol (in Coplin's jars) for five to ten minutes to remove paraffin.

16. Place sections in absolute alcohol for five minutes.

17. Place sections in 95 per cent. alcohol for five minutes.

18. Place sections in 80 per cent. alcohol for five minutes.

19. Place sections in water for five minutes.
20. Place sections in hematoxylin for five minutes.
21. Place sections under a slow stream of running water until they turn blue.
22. Place sections in a weak aqueous solution (about 1 per cent.) of eosin.
23. Place sections in 80 per cent. alcohol for a few seconds.
24. Place sections in 95 per cent. alcohol for a few seconds.
25. Place sections in absolute alcohol for a few seconds.
26. Place sections in xylol for ten or more minutes (to clear).
27. Mount in balsam.

Normally, in the slides from the aspirated fasting residue one finds occasional epithelial cells; occasional leukocytes with protoplasm intact in those cases in which chemical titration shows faintly acid or neutral or slightly alkaline reaction. Boas and Paul Cohnheim have pointed out that digested protoplasm of epithelium or leukocytes indicates the presence of free hydrochloric acid and pepsin. When the protoplasm of the epithelial cells is still intact it is possible to differentiate endogenous gastric cells and those originating from the mouth, pharynx, respiratory track, and esophagus. Normally, one frequently encounters the snail-like bodies, first described by Jaworski,[2] which Boas and Paul Cohnheim believe to be mucus, which have been acted upon by hydrochloric acid. If there has been regurgitation from the duodenum there may be crystals of some of the bile salts.

Pathologically, in the fasting morning stomach one may find remnants of food eaten the night before, such as muscle fibers still striated or partially digested; starch granules; vegetable cells; seeds from berries, any of which from the twelve-hour fasting stomach is indicative of motor insufficiency, due either to pyloric obstruction or rarely to advanced atony. Associated with this, if one finds sarcinæ in numbers or many yeast cells in process of germination it would suggest gastric dilatation with stagnation and fermentation. Sarcinæ are rarely found in the ectasia of cancer, except the ulcus carcinomatosum type. It should be remembered that small amounts of food remnants are not significantly pathological (cryptic mucosæ and cavities in teeth).

Paul Cohnheim attaches importance to infusoria like Trichomonas hominis and Megastoma entericum, and believes they are associated with cancer when the motility of the stomach is not affected. Personally, I have never encountered them. They require for their development an absence of hydrochloric acid, an alkaline medium, and a cryptic mucosa. Mucus from the respiratory track will float, owing to its air content. Microscopically, it is characterized by containing alveolar cells and myelin drops, while columnar epithelium indicates its derivation from the gastric mucous membrane. Also, in gastric dilatation one occasionally encounters spores and mycelial cells from vegetable moulds. Leukocytes are indicative of an inflammatory reaction. It has been stated that if they occur in large numbers it is strongly suggestive of phlegmonous or suppurative gastritis, an extremely rare condition. It has been my experience, however, to find large numbers of leukocytes in all cases of gastric ulcer, in many of the simple forms of gastritis in the inflammatory or congestive stage, and in cancer of the stomach, affecting chiefly the glandularis. Pathologically, a significant finding is the presence of Oppler-Boas bacilli, which most usually occurs in the subacid or anacid gastric juices, associated with retention and stagnation. Most commonly the presence of lactic acid is readily demonstrable when these bacilli are found. Their presence has so often been seen to be associated with cancer of the stomach as to be extremely suggestive of this condition, but by no means pathognomonic. They are large non-motile bacilli with a somewhat typical morphological arrangement in long chains, and are readily differentiated from the Leptothrix buccalis by acting negatively to Gram's stain. In gastric sediments prepared as above described they have a tendency to arrange themselves in dense masses, interlaced with one another, and resemble hair-like balls when viewed under a low-power microscope.

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[2] Münch. med. Wchnschr., 1887.

The normal stomach should contain very few bacteria, and when they do occur in large numbers it has been considered to be due to a gastric juice poor in antiseptic property. I believe when the bacterial flora of the stomach is found high that one is dealing with a distinctly pathological condition. The most common normal invader of the stomach is the Bacillus coli group, but the appearance of diphtheroid bacilli, staphylococci, and particularly various types of streptococci indicates trouble. Here, too, one meets with a pathologically increased number of leukocytes.

It is surprising how often small isolated fragments or flakes of gastric mucosa will be recovered by this method. Minute particles, barely of macroscopic size, which would readily escape detection in the lavage water, may prove to be the one point upon which the correct diagnosis can be made. Furthermore, it is often possible, from a microscopic study of these bits of mucosa, to determine from which segment of the stomach they come, whether the fundic, prepyloric, or antrum pyloric, bearing in mind the anatomical distribution of the different types of glands. Microscopically, these minute fragments may show only the peripheral portion of the villus, extending down to various depths through the glandularis, while in the larger fragments the entire width of the mucosa, at times including the muscularis mucosæ, will be found. It is often possible to differentiate accurately the following conditions:

Cancer of the Stomach. It is not uncommon to find (see Cases III and IV, Figs. 4 and 8) fragments of gastric mucosa which show gastric tubules with broken basement membranes and atypical invasive proliferation of the epithelial cells through the interglandular stroma, and other glands may show various types of degeneration, parenchymatous, mucoidal, vacuolary, or atrophic. In all these retrogressive degenerations the staining reactions are poor as compared with the progressive carcinomatous changes. If the fragment of mucosa extends down to the submucosa, finger-like processes of carcinomatous invasion affecting the fundic portions of glands, or even collections or nests of carcinoma cells involving the lymphoid tissue, often showing beautiful mitotic figures, may be found. There is almost invariably a well-marked leukocytic infiltration of the interglandular stroma, frequently associated with pyogenic bacteria, particularly streptococci. When bits of mucosa with recognizable glandular elements can not be found, one may frequently see microscopic fields showing areas of necrosis, plentifully studded with polynuclear leukocytes and invaded by bacteria. Often in the centre of these eosin-stained areas of necrosis may be seen masses of granular amorphous-like debris, staining heavily with methylene blue or hematoxylin, which suggests the remains of degenerated epithelial cells, carcinomatous or other, in all stages short of coagulation necrosis (see Figs. 2, 3 and 5). One finds the bacteria massed chiefly at this point, the degenerated cells evidently furnishing an excellent pabulum. Around these necrotic areas will frequently be found immense numbers of Oppler-Boas bacilli, often arranged in such dense clusters of interlaced bacteria as to resemble balls of hair when viewed under low power (see Figs. 2, 3 and 5).

Occasionally one will find fairly large clusters or nests of recognizable cancer cells, often in number up to 100 cells, as in Case I of this series (see Fig. 1). In cancer cases with pyloric obstruction the twelve-hour fasting stomach sediment will show various food rests, meat fibers, vegetable cells, starch granules, fat droplets, or crystals, and if there is fermentation, yeast cells in abundance. Red-blood corpuscles may occasionally be found intact, more commonly in various stages of crenation, and most frequently as hematin crystals. Crystals of bile salts may also be found.

Even if definitely diagnostic isolated cancer cells or bits of mucosa showing carcinomatous degeneration can not be found, the presence of areas of necrosis showing leukocytic infiltration and bacterial invasion will strongly suggest either gastric cancer or gastric ulcer. If Oppler-Boas bacilli are present and the chemical analysis of the gastric juice approaches the subacid or anacid curves the diagnosis points more particularly to cancer (see Chart I, Case IV). A positive Wolff-Junghans reaction would support this point of view.

It is, of course, understood that, as a rule, these laboratory findings are the tail to the kite as compared to a carefully taken anamnesis, physical examination, and a critical clinical scrutiny of the case; but coupled with the latter they may prove to be the turning-point in the diagnosis, and, indeed, it not unfrequently occurs that the diagnosis is definitely pathologically made by the finding of recognizable cancer cells (see Cases I, III, and IV, Figs. 1, 4, and 8).

GASTRIC ULCER. While it is more difficult here to make a definitely pathological diagnosis from a gastric sediment study, nevertheless the finding of areas of necrosis with numerous leukocytes and pyogenic bacteria indicates the presence of an ulcerative process whether superficial or deep. The absence of Oppler-Boas bacilli is likewise suggestive. If coupled with this there are bits of the glandularis mucosæ showing the gastric tubules well marked and the cells reacting sharply to the differential stains and the interglandular stroma invaded by leukocytes, the likelihood of this diagnosis would be increased (see Fig. 10). Here, too, one frequently encounters isolated exfoliated epithelial cells, particularly the border or cover cells, reacting well to eosin, either intact or showing granular degeneration. A normal or hyperchlorhydric fractionation curve of the gastric juice, especially when associated with the presence of occult blood, would support this contention. It should be thoroughly borne in mind, however, that the presence of occult blood by no means always indicates ulcer or cancer, it being so frequently encountered in superficial erosions, in states of chronic passive congestion with a friable gastric mucosæ, and in many cases of achylia gastrica, as recently pointed out by J. T. Pilcher[3] in a series of cases studied at the Mayo Clinic.

CHRONIC GASTRITIS. In hypertrophic glandular gastritis and gastritis acida the pathological diagnosis depends upon the finding of fragments or flakes of mucous membrane presenting a well-marked hyperplasia of the glandular elements, with the cells showing good staining power. This applies most particularly to the base or fundic portion of the glands, whereas the cells toward the periphery will often show granular degeneration, loss of staining power, and absence of nuclei. This peripheral portion frequently desquamates or sloughs off and is found in isolated areas of the microscopic field (see Fig. 7). The interglandular stroma is seen to be infiltrated with an increased number of leukocytes of the lymphoid type in the more chronic processes and a predominance of polynuclear varieties in the acute stages. The venules are usually enlarged or dilated, and areas of pigmentation and congestion may be seen.

ATROPHIC GASTRITIS. Here recoverable bits of gastric mucosa will show a considerable diminution in number of the gastric tubules, with marked irregularity in their distribution; their alignment is very imperfect and few glands can be traced from fundus to neck. The cells stain poorly and show mucoid and fatty degeneration, with marked vacuolization. Frequently, cells are seen separating or completely broken off from the basement membrane and lying in the lumen of the tubule. In fact, all of the epithelium may be completely denuded from the tubule, leaving empty spaces in the mucosa.

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[3] Jour. Amer. Med. Assoc., November 19, 1910.

The leukocytic infiltration is usually of the lymphocytic type, and areas of venous congestion are relatively infrequent. In the same microscopic field, or in other portions of the sediment in the same case, may be found bits of mucosa showing practically normal glandular elements, and it may be rightfully argued that the findings of such microscopic fragments of the mucosa showing various pathological states may not represent a true picture of the amount of organic damage or degree of functional power of the stomach as a whole. Nevertheless, the above findings, associated with the study of the fractionation curves, will often corroborate or point out the clinical diagnosis.

Achylia Gastrica. In the recovery of bits of mucous membrane in casés of this type the noteworthy features have been the pronounced reduction in the number of glandular tubules in various stages of benign degeneration (Fig. 9, Case V). These degenerations consist chiefly of the mucoid type, which is probably a later stage of a simple parenchymatous degeneration. Later cystic dilatations appear, and in some cases there occurs rupture of basement membranes with atypical epithelial proliferation, showing a tendency to invade the surrounding stroma. Such cases should be most carefully investigated, and repeated attempts to recover additional mucosal fragments should be made, as it may prove to be a transitional stage between a benign and an early malignant achylia. Particularly in these cases does the Wolff-Junghans reaction offer a possible means of differentiation. In all this group of cases there is a marked increase in connective tissue in the interglandular stroma, and at times wide bands of it may be seen separating small islands of degenerated tubules. Indeed, it is possible that this connective tissue overgrowth in the benign achylias may be a forerunner of that rare condition Linnitis plastica. The depth of the glandularis is strikingly diminished, and it is not uncommon to find that a single low-power microscopic field takes in the entire depth and width of the glandularis, including the muscularis mucosæ, at which point rupture most commonly occurs. At the peripheral portion of the glandularis may be seen dilated venules markedly congested and with extravasation or diapedesis of red-blood corpuscles, which explains the occasional (frequent?) demonstration of occult blood.[4] At the peripheral portion, too, may be found a deep layer of mucus, and islands of mucus may also be seen in isolated portions of the sections.

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[4] Cf. Pilcher, Jour. Am. Med. Assn., November 19 1910.

When one is successful in recovering fragments of mucosa showing these pathological changes it checks up nicely the fractionation curves of the achylic type and would serve to differentiate between the psychical achylia occurring during the first stage of digestion and the total chemical achylia persisting throughout the entire digestive cycle (see Chart II, Case V).

GASTRIC ATONY WITH DILATATION. In the early cases the sediment returns are usually negative save for amorphous debris and patches of mucus in which are enmeshed occasional leukocytes. In the more advanced cases with benign motor insufficiency are found various food rests even on a twelve-hour fasting stomach, although it is uncommon to find this unassociated with some degree of pyloric stenosis.

GASTRIC DILATATION WITH FERMENTATION. In cases of gastric dilatation with fermentation one will frequently find in addition groups of sarcinæ, germinating yeast cells, spore-bearing fungi, and mycelial threads. Bacteriologically, many groups of organisms may be represented, chiefly, however, of the spore-bearing type.

HYPERSECRETION CONTINUA (REICHMANN'S DISEASE). Oftentimes the sediments are practically negative except for a granular amorphous debris with crystalline deposits of bile salts. If there is an associated inflammatory condition (a gastritis), one will find the nuclei of numerous leukocytes with protoplasm digested as well as free nuclei from exfoliated epithelial cells. In the inflammatory types under oil immersion can frequently be made out a marked increase in the bacterial flora. Since so many cases of hypersecretion are found associated with gastric dilatation sequential to either atony, pylorospasm, pyloric stenosis, or chronic appendicitis, food rests may be frequently encountered.

ESOPHAGEAL SEDIMENTS. Similarly, in douching the esophagus by this method one may recover esophageal sediments of diagnostic import, as in cases of cardiospasm with esophageal dilatation. In cases of esophageal cancer, minute bits of tissue containing nests of cancer cells may be found, together with necrotic debris, studded with leukocytes and invaded by bacteria. In cases of esophagitis following the ingestion of corrosive poisons there may be recovered bits of necrotic mucosa showing a high degree of ulcerative inflammation. It is noteworthy that in cardiospasm, and I believe this to be pathognomonic of this condition, it will be found possible to douche the esophagus and recover from the esophagus all of the lavage fluid introduced without having to pass the tube into the stomach. (This point has been repeatedly demonstrated in a case which will be reported in full at an early date.)

CONCLUSIONS. 1. The routine study of gastric sediments will be found to give information of both diagnostic and prognostic importance.

2. In those cases in which are recovered fragments of mucosa showing pathological alterations the clinical diagnosis may be checked up or supported as in no other way short of surgical exploration. This is notably the case in cancer of the stomach involving the glandularis. One may be rewarded by positive findings in comparatively early cases of cancer, which are clinically of the borderline type.

3. In clinically doubtful or obscure cases exhibiting gastric symptoms a study of one or several slides of gastric sediment may reveal sufficient pathological evidence to point correctly the diagnostic accusing finger.

4. A single pathologically negative sediment means nothing, and is to be regarded in the same way as failure to recover tubercle bacillus from the sputum of patients clinically tubercular.

5. Repeated pathologically negative sediments in a given case argues strongly in favor of functional rather than organic gastric disease.

6. When organic disease is strongly suspected, notwithstanding repeated pathologically negative sediments, one should critically survey the technic of obtaining and preparing the specimen.

I desire to acknowledge the courtesy of Dr. John B. Deaver, in the use of hospital notes on some of his patients on whom these studies were made, and to express my thanks to Dr. Carl E. Becker, of the pathological laboratory of the German Hospital, and to Mr. John Eiman, of the pathological laboratory of the Methodist Hospital, for their cordial coöperation and their painstaking care in the preparation of the specimens.

REPORT OF CASES.

Case I (Carcinoma of the Stomach).—H. F., aged sixty-two years; married; occupation, machinist.

Chief Complaint. Indigestion, with vomiting and constant pain in the stomach.

Present Illness. Four months ago he began to get pain in his stomach, occurring two to three hours after meals and relieved by eating. This relief would last for two hours and then the pain would begin again. About the same time he began to get attacks of vomiting; says he never vomited blood, but has vomited dark brown material. Associated belching and water brash. Constipated. No jaundice. Has lost fifty pounds in weight in the last nine months.

Past Medical History. Never sick before. No history of venereal diseases.

Social History. Smokes and uses beer moderately. Has always been a hard-working man, with regular habits.

Family History. Wife and four children living and well. No family history of cancer.

Physical Examination. Undernourished adult male, with no evident pain or distress. Eyes, ears, and nose negative. Tongue rather beefy red. Teeth in poor condition with pyorrhea. Neck: a few palpable cervical lymph glands. Skin slightly anemic and cachectic, with considerable emaciation.

Lungs: Small, moist rales at the posterior left apex and a few rales over the right lung posteriorly. Slight impairment of resonance at the left apex.

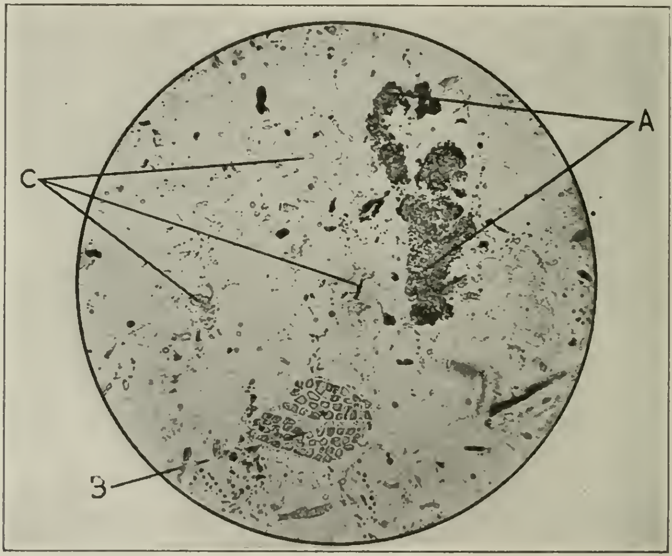


Fig. 1.—Nest of cancer cells from Case I, H. F., aged sixty-two years. Free HCl, 0; total acidity, 8. Occult blood positive. Lactic acid negative. Oppler-Boas bacilli not found. Wolff-Junghans reaction positive in $\frac{1}{320}$ dilution. *A*, nest of cancer cells; *B*, bundles of striated muscle fibers from retained food residue; *C*, necrotic debris with streptococcic invasion. × 100.

Heart: Normal in size and position. Sounds are free from murmurs and accentuations, but first sound at the apex is of poor muscular quality and can scarcely be heard. Peripheral blood-vessels sclerotic.

Blood-pressure: Systolic, 160; diastolic, 78.

Abdomen: Walls thin; tenderness in epigastrium, especially just left of the midline. A sense of resistance can be felt in this area—almost like a movable mass. Abdomen otherwise negative.

Extremities and genitalia negative.

Gastric Analysis: Sixty minutes after Ewald breakfast. Quantity, 90 c.c. Brownish yellow, putrid odor, faintly alkaline. Bile negative. Occult blood positive to benzidine and slightly positive to guaiac. Free HCl absent; total acidity, 8; lactic acid absent.

Microscopically: A few starch granules partially digested; granular debris. Oppler-Boas bacilli absent. Wolff-Junghans reaction positive in dilution 1 to 320.

Gastric Sediment: Shows nest of cancer cells. Necrotic debris, and food rests on six hour fasting stomach (see Fig. 1).

Stool: Grayish-green; semisolid; moderate amount; characteristic odor; alkaline reaction. Bile positive. Occult blood positive to benzidine and to guaiac.

Microscopically: Bile-stained vegetable cells; fatty acid crystals and crystals of triple phosphate; granular debris and bacteria.

Blood Count: Hemoglobin, 58 per cent.; red-blood cells, 3,890,000; color index: 0.76; white blood-cells, 11,400.

Differential Count: Polymorphonuclear neutrophiles, 76 per cent.; lymphocytes, 24 per cent.; large mononuclears, 0; transitionals, 0; eosinophiles, 0; total, 100 per cent.

Fluoroscopic Examination: Stomach not markedly ptotic or dilated. No absolute mass, but there is some slight increase in density toward the cardiac end of the greater curvature.

Operation January 9, 1913 (Dr. Deaver). Upper right rectus incision. Stomach exposed. A hard mass was found on the entire lesser curvature extending to the greater curvature and involving the great omentum. Type is scirrhus. Radical cure not possible. Usual closure of wound. Dry dressing.

CASE II (Carcinoma of the Stomach).—J. G., aged sixty-four years; married; occupation, cement finisher.

Chief Complaint. Constant pain in epigastrium; loss of weight; anorexia; constipation.

Present Illness. Two months prior to admission he developed distress in the gastric area, occurring immediately after meals, with a sense of weight in the epigastrium. "The food seems to lie in my stomach and does not pass out." He has had to lie down on account of weakness after each meal, has difficulty in breathing, and has a constant gnawing pain in the epigastrium, without reference to eating. The pain does not keep him awake at night. His appetite has dwindled so that he can eat very little, and he relishes only liquids and oatmeal. He can not digest any meat and is violently constipated, using drastic cathartics every day. He has never vomited; he has never noticed any blood in his stools, but they have lately been of a dark, blackish-brown color. He, himself, found a lump in his epigastrium about six weeks ago that he thinks is growing larger. He has lost twenty pounds in five weeks.

Family History. Wife and three children living; one died in infancy: one of appendicitis and one of epilepsy. No history of cancer, tuberculosis, or hemophilia.

Past Medical History. Unimportant.

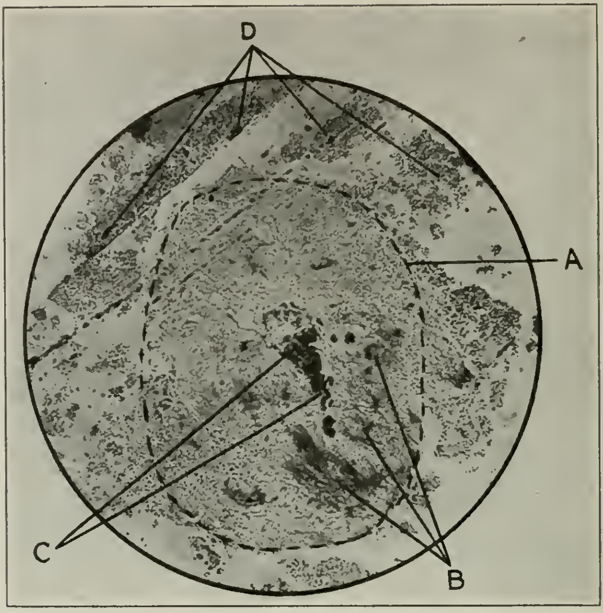


Fig. 2.—Gastric sediment from Case II, J. G., aged sixty-four years, showing necrotic debris and masses of Oppler-Boas bacilli and large numbers of leukocytes. *A*, necrotic debris; *B*, masses of Oppler-Boas bacilli; *C*, necrotic carcinomatous debris; *D*, collections of leukocytes. × 100.

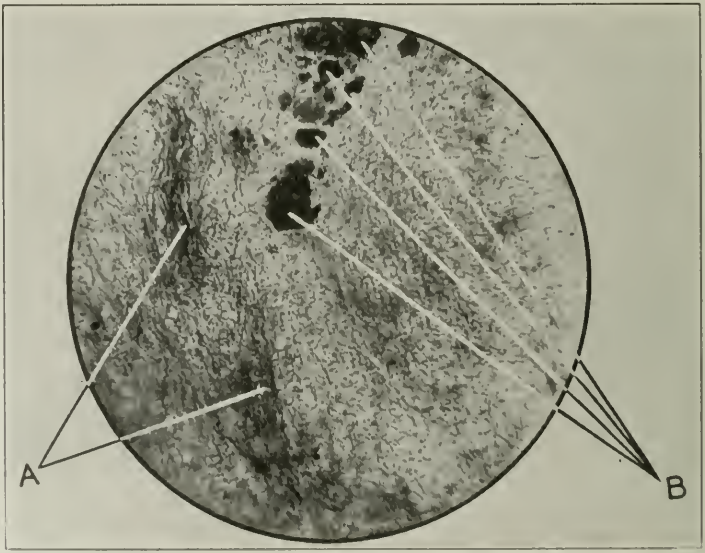


Fig. 3.—Oil immersion of Fig. 2, showing masses of Oppler-Boas bacilli. *A*, masses of Oppler-Boas bacilli; *B*, necrotic carcinomatous debris. × 800.

Social History. Denies venereal disease; smokes moderately; does not use alcohol.

Physical Examination. Emaciated adult male in no great pain. Eyes and nose negative. Ears: left, negative; right, quite deaf. Mouth: mucous membranes pale. Teeth: decayed and missing. Tongue: clean and furrowed.

Chest: Heart and lungs surgically negative.

Abdomen: Muscular, difficult to palpate; peristalsis poor; some distention; no rigidity. Mass present, beginning 5 cm. below the xiphoid, extending 4 cm. to the right of the midline and 2.5 cm. to the left of the midline; is hard, resistant, moves slightly downward on deep inspiration, and seemingly involves greater curvature throughout; pain not present on deep palpation. Otherwise abdominal examination is negative except for left inguinal hernia. Genitalia and extremities negative. Blood-pressure: systolic, 140; diastolic, 70.

Blood Count: Hemaglobin, 72; red-blood cells, 4,740,000; color index, 0.76; white-blood cells, 7155.

Differential Count: Polymorphonuclear neutrophiles, 53 per cent.; lymphocytes, 23 per cent.; large mononuclears, 16 per cent.; transitionals, 5 per cent.; eosinophiles, 3 per cent.; total, 100 per cent.

Stool: Yellowish brown; normal consistency; moderate amount; characteristic odor. Alkaline reaction. Bile strongly positive. Occult blood faintly positive to benzidine and negative to guaiac.

Microscopically: Bile-stained vegetable cells, mucus, and debris. Free fat globules and bacteria.

Urinalyses: Unimportant.

Fluoroscopic Examination. Lower border of the stomach reaches to the umbilicus. Shadow of a dense mass apparently involving the greater curvature.

Gastric Sediment Study: Shows a large amount of necrotic debris with degenerated epithelial cells with enormous collections of Oppler-Boas bacilli, particularly surrounding the necrotic epithelial debris, and very large numbers of leukocytes, chiefly polynuclear, with protoplasm intact (see Figs. 2 and 3).

Operation December 4, 1912 (Dr. Deaver). Upper right rectus incision. Large mass found involving the anterior wall of the stomach and extending up to the cardia. Carcinomatous invasion of the mesentery and pancreas. Case inoperable. Wound closed.

Case III (Carcinoma of the Stomach).—S. H., aged fifty-nine years; married; occupation, scale maker.

Chief Complaint. Vomiting and pain after eating and belching.

Present Illness. Six months ago had an attack of severe hiccoughing, with chills, lasting five days and associated with vomiting. He has never felt well since that time. Appetite lessened, and for the last six weeks has had attacks of vomiting, occurring three to

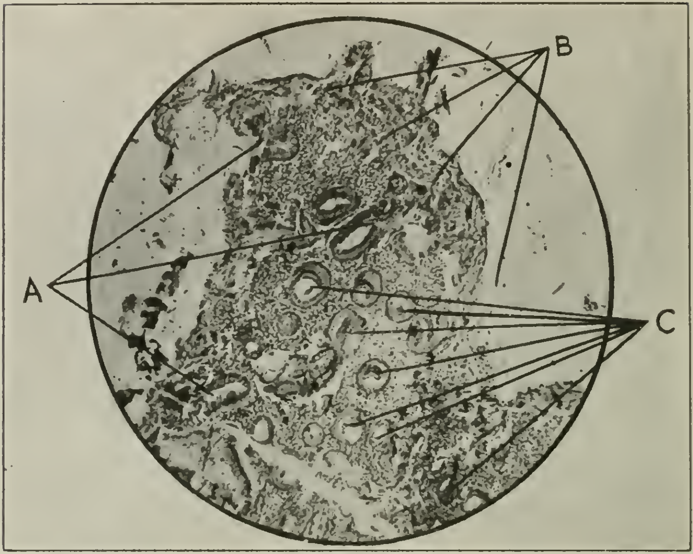


FIG. 4.—Fragment of gastric mucosa showing carcinomatous degeneration. Case III, S. H., aged fifty-nine years. Free HCl, 0; total acidity, 52. Lactic acid positive. Occult blood positive. Oppler-Boas bacilli present. *A*, rupture of basement membrane and a typical proliferation of epithelium; *B*, carcinomatous degeneration; *C*, gastric tubules in various stages of atrophy. × 100.

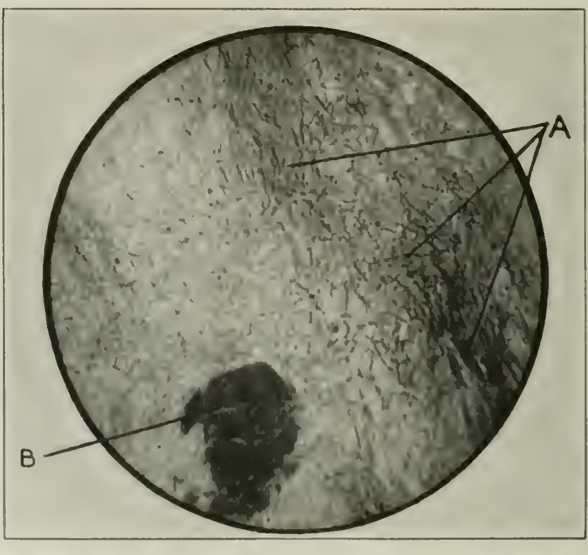


FIG. 5.—Gastric sediment. Case III, S. H., aged fifty-nine years, showing large numbers of Oppler-Boas bacilli. *A*, Oppler-Boas bacilli; *B*, necrotic cancer cells. × 800.

four hours after eating. No definite retention vomiting, nor has he vomited bloody or blackish material. He does not have much pain before vomiting, but says he feels as though the food was being rolled up into a ball and vomiting gives relief. The pain is not referred to the back, but it is located in the epigastrium and over the gall-bladder. He has noticed that the pain waked him up at night when sleeping on his right side. He has lost twenty pounds in weight in six months. He has much gaseous distention of the stomach and belches a great deal. He has pyrosis but no water brash; has not been jaundiced. Bowels are constipated; no melena. Condition has improved a little during the past two weeks.

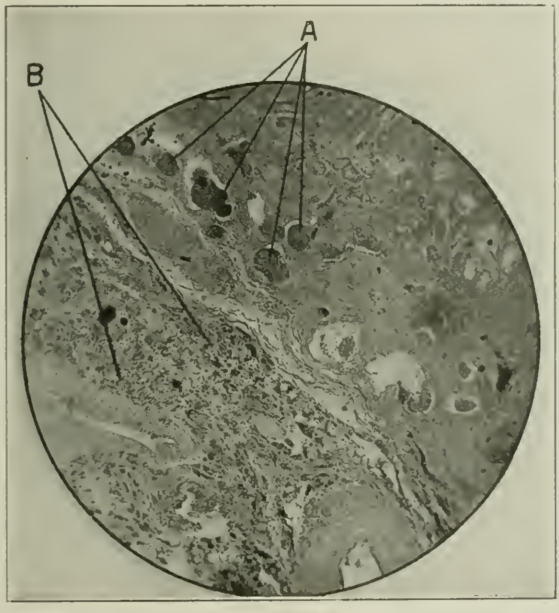


Fig. 6.—Postoperative section (subtotal gastroectomy) from gastric mucosa of Case III, S. H., confirming diagnosis of cancer. *A*, nest of cancer cells in muscularis mucosæ; *B*, infiltration of leukocytes. × 100.

Past Medical History. "Gastric fever" six years ago. Indefinite history difficult to interpret.

Social History. Uses alcohol moderately.

Family History. Unimportant.

Physical Examination. Somewhat emaciated looking; skin pale; eyes, ears, nose, and mouth negative. Lungs surgically negative.

Abdomen: Scaphoidal. Skin: thin and lax muscular walls. No masses detected. Deep palpation elicits diffuse epigastric tenderness, with distinct muscle spasm and tenderness over McBurney's point, but not over the gall-bladder. Otherwise abdomen is negative.

Genitalia and extremities: Negative.

Blood-pressure: Systolic, 112; diastolic, 90.

Blood Count: Hemaglobin, 77; red-blood cells, 4,360,000; color index, 0.89; white blood cells, 8500.

Differential Count: Polymorphonuclear neutrophiles, 63 per cent.; lymphocytes, 32 per cent.; large mononuclears, 1 per cent.; transitionals, 4 per cent.; total, 100 per cent.

Gastric Analysis: *Full Meal* (six-hour stomach): 375 c.c. recovered; light brown color; aromatic odor. Bile: negative. Occult blood, 0; free HCl, 0; total acidity, 44; lactic acid, faintly positive.

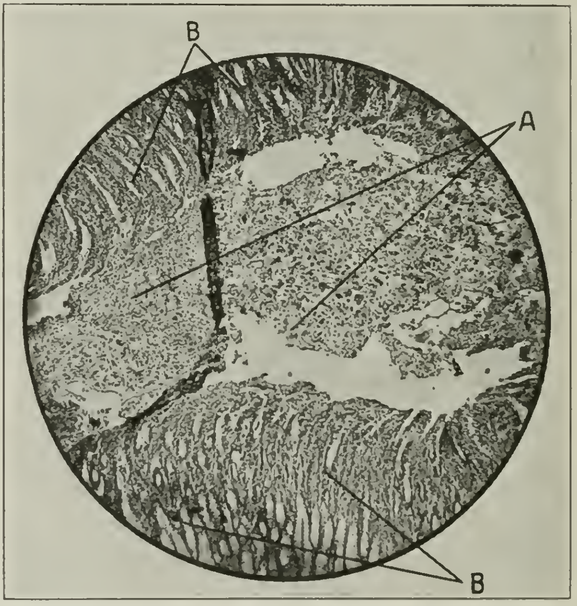


Fig. 7.—Gastric sediment of fragment of gastric mucosa from case of gastritis acida and hypersecretion. S. H., aged fifty-nine years, showing *A*, inflammatory debris containing many polynuclear leukocytes sloughing off between *B*, two folds of mucous membrane. × 100.

Microscopically. Oppler-Boas bacilli present. Granular debris; a few free fat globules and partially digested starch granules and mucus plus.

Ewald breakfast (sixty minutes): 130 c.c. recovered; yellowish-brown, aromatic odor; bile negative. Occult blood: strongly positive to benzidine and negative to guaiac. Free HCl, 0; total acidity, 52; lactic acid, positive.

Microscopically: Oppler-Boas bacilli; fat globules; partially digested starch; granular debris.

Cammidge "C" reaction: Positive.

Stool Analysis: Greenish-brown; fluid and small fecal masses; neutral reaction; bile strongly positive; occult blood strongly positive to benzidine. Guaiac negative.

Microscopically: Bile stained vegetable cells; few fat globules; debris and bacteria.

X-ray Reports: Stomach dilated but not markedly ptosed; lowest border one-half inch below navel; there is an obstruction to the flow of bismuth at the pylorus which shows marked density, presumably from a growth. No other masses detected.

Gastric Sediments: Show fragments of gastric mucosa, with areas of carcinomatous degeneration and gastric tubules in various stages of atrophy (see Fig. 4) and other areas showing necrotic cancer debris surrounded by masses of Oppler-Boas bacilli (see Fig. 5).

Operation February 1, 1913. Upper right rectus incision. Carcinomatous mass at pylorus and duodenum, involving lesser curvature more than the greater. Head of pancreas hardened. Partial gastrectomy and duodenectomy, removing carcinomatous mass. Posterior gastro-enterostomy. Considerable hemorrhage. Two pieces of gauze to stomach bed for drainage. Usual closure of wound at point of drainage. Patient in bad shape on table and transfused with 3000 c.c. of saline, and immediately after leaving operating room was again transfused with 1500 c.c. of saline; given active stimulation and oxygen, with no avail. Patient died of shock.

Culture: From interior of stomach at operation: Bacillus coli communis.

Pathological Report: Portion of stomach 12 cm. x 9 cm. and 4 cm. thick. Stomach hard and wall thickened. Omental attachment at greater curvature shows two hardened glands, also at lesser curvature. Inner surface of stomach is injected, granular, and shows projecting firm nodules; wall of pylorus is thickened and hard, and cut surface is pale, hard, and resembles gristle.

Microscopically: Adenocarcinoma; scirrhus with metastasis to gastric glands (see Fig. 4).

Case IV (Cancer of the Stomach).—H. M., aged forty-five years; occupation, leather worker.

Chief Complaint. Pain in the stomach and vomiting.

Present Illness. For ten months has been troubled with pain in the stomach and vomiting. Pain is at times sharp and at other times dragging and heavy; is worse at night when he lies down; sometimes relieved by eating and sometimes not; pain is nearly always present to some extent; does not vomit except when pain has been severe; vomiting has been distinctly of the retention type; pain does not radiate; has never been jaundiced; bowels constipated; has lost fifteen pounds.

Past Medical History. Usual diseases of childhood; denies venereal history.

Social History. Irregular habits; uses alcohol at times to excess. Always more or less constant. Smokes a pipe.

Family History. Mother and two brothers died of pneumonia and father of apoplectic stroke.

Physical Examination. Fairly well-nourished adult male; hair thin and gray. Tongue clean; no tremor. Eyes, ears, nose, negative. Lungs and heart negative. Abdomen flat; walls lax; visible peristalsis seen at times. Increased resistance over recti muscle in upper abdomen. Area of liver dulness small. No mass detected. Extremities negative August 4, 1913. During the passage of the stomach tube, patient vomited large quantities of food eaten eighteen hours ago, probably 1500 c.c., of a sour, fermenting odor like cider. Free HCl, 32; combined, 20; total acidity, 76. Occult blood, negative. No inflation of lower border found at the level of the navel.

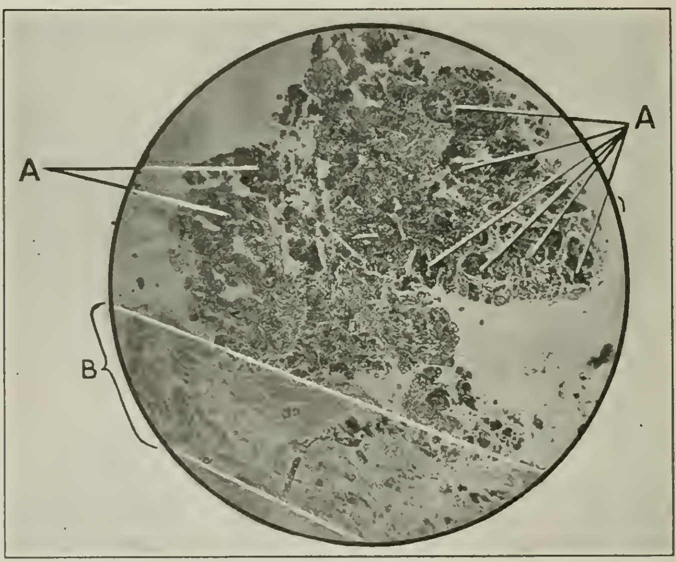


Fig. 8.—Fragment of gastric mucosa from Case IV, H. M., aged forty-five years, showing a carcinomatous degeneration. *A*, carcinomatous degeneration of gastric tubules; *B*, submucosa. × 100.

August 9. Blood count: hemoglobin, 64 per cent.; white-blood cells, 7200. Stool, brownish-black; semiformed; bile strongly positive; occult blood strongly positive to benzidine; negative to guaiac.

August 20. Wassermann reaction negative.

August 19. Fluoroscopic Examination (with 80 gm. bismuth subcarbonate). Moderate gastrectasis; lowest border of stomach is two and a half inches below the navel; sluggish peristalsis; no mass detected. Full meal removed in seven hours. 230 c.c. of brownish-yellow, sour-smelling chyme; increased intimately mixed mucus; bile negative. Occult blood positive to benzidine; negative to guaiac. Free HCl, 53; total acidity, 95. Butyric acid positive.

Microscopically: Some undigested starch; free fat globules; epithelial cells; no Oppler-Boas bacilli.

August 22. Ewald breakfast removed in sixty minutes by aspiration bottle and over 500 c.c. of mixed contents recovered. Bread crumbs and water plus prune pulp, coagulated casein, and albumen from milk and eggs from night of August 21. Mucus plus; sour odor. Free HCl, 12; combined HCl, 0; total acidity, 30; occult blood negative in filtrate. Butyric acid positive. Starch digestion to maltose.

Microscopically: Starch granules; meat cells; sarcinæ; free fat globules; no Oppler-Boas bacilli.

Gastric Sediment, August 22. Fragment of gastric mucosa shows tubules in various stages of atrophic degeneration, with areas of carcinomatous degeneration showing an invasive tendency; high grade leukocytic infiltration; no bacteria demonstrable (see Fig. 8).

Operation advised but declined until two months later (October 6), when patient was referred to the surgical wards with an increase in symptoms and continued loss of weight.

Operation, October 8, 1913 (Dr. Deaver). Upper right rectus incision. Stomach was brought up and a mass found involving the pylorus and head of the pancreas. Posterior gastro-enterostomy was done in the usual way. Patient left the table in poor shape but reacted well to a transfusion of 2000 c.c., and was discharged from the hospital October 20.

October 6, 1914. When seen today at the Jefferson Hospital Clinic, one year after his operation, it was learned that for nine months following the gastro-enterostomy the patient had shown marked improvement in symptoms with the cessation of his retention vomiting and a gain in weight from 116 to 160 pounds. About three months ago his appetite began to fail; he began to lose weight; his symptoms of sour stomach and retention vomiting returned. Lavage today shows overnight retention. On physical examination there is a large palpable mass, about the size of a small orange, in the upper right epigastrium, about an inch and a half to the right of the midline. Liver is enlarged, the lower edge being palpable two finger-breadths below the costal margin in the mammillary line; edge rounded; upper border of liver dulness extends to the fourth interspace.

October 22. Ewald breakfast aspirated at sixty minutes; 100 c.c. of reddish-brown bread crumbs and debris, having an aromatic odor with macroscopic blood spots and great increase in intimately mixed mucus. Free HCl, 20; combined HCl, negative; total acidity, 20. Occult blood strongly positive. Starch digestion to maltose.

Microscopically: Red blood cells; starch granules; no Oppler-Boas or other bacteria.

Wolff-Junghans reaction: Positive in 1 to 80 dilution but negative in higher dilutions.

December 22, 1914. Fractional analysis of Chart I.

Patient referred to medical wards of Jefferson Hospital October 22, where he remained until his death, March 25, 1915, twenty months after the diagnosis by gastric sediment study had been made. During the weeks prior to his death there was a rapid advance in his cachexia, anemia, and the increase in his liver dulness, with the appearance of jaundice, six weeks before he died and subsequently the development of abdominal ascites, due to blockage of his portal circulation.

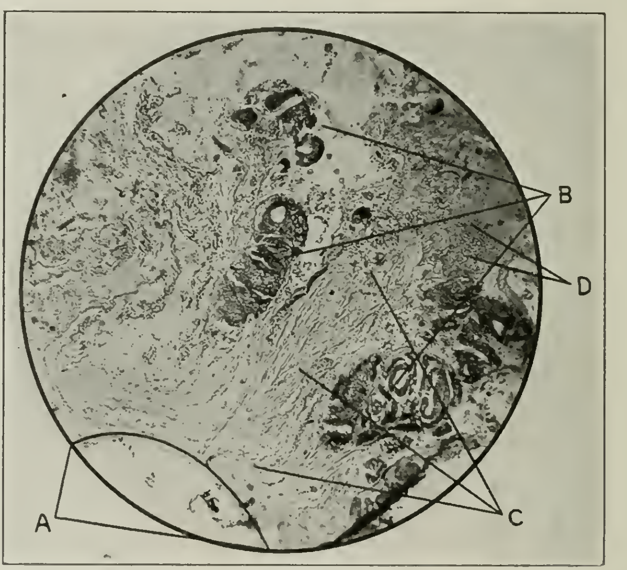


FIG. 9.—Gastric sediment showing fragment of mucosa of the human stomach in a case of advanced, atrophic gastritis. (Achylia gastrica, Case V, Mrs. A. H.) *A*, muscularis mucosæ at point of rupture; *B*, gastric tubules in various stages of atrophic degeneration; *C*, increase in interglandular connective tissue; *D*, area of conjestion. × 100.

At autopsy a mass was found involving the pylorus and the greater curvature, the greater omentum and the head of the pancreas, and there were extensive metastases to the mesenteric and retroperitoneal glands and to the parietal peritoneum of the abdominal wall and the under surface of the diaphragm. The liver was enormously enlarged, particularly upward. The upper border was found pushing up the diaphragm to the second interspace, and the right lung was collapsed and undergoing pressure atrophy. The liver was everywhere studded with carcinomatous nodules, in various stages of necrosis. The gall-bladder likewise showed metastases. There were about eight quarts of straw-colored fluid in the abdominal cavity. The gastro-enterostomy opening was markedly narrowed, due to the advanced carcinomatous process along the greater curvature. The stomach was enormously dilated, and when cut open was found to contain about a pint of dark chocolate-brown granular debris, foul smelling, from which further sections were prepared which show desquamated epithelium extensively invaded by cancer.

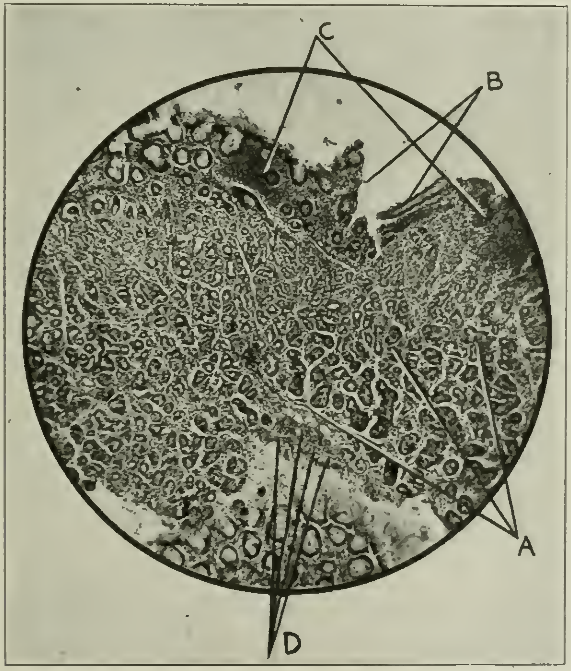


Fig. 10.—Fragment of mucosa from a case of gastric ulcer with free HCl, 86; combined HCl, 21; total acidity, 110. Occult blood positive. *A*, glandular hyperplasia; *B* area of superficial erosions; *C*, area of conjestion (occult blood positive); *D*, areas of leukocytic infiltration. × 100.

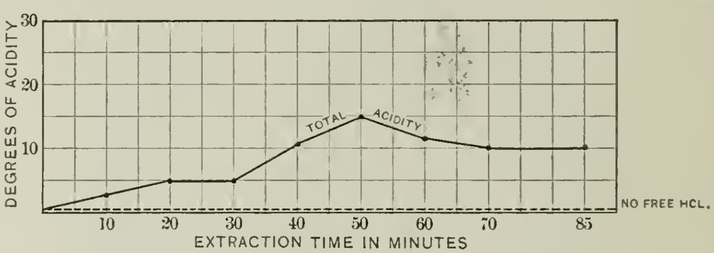
Case V (Achylia Gastrica).—Mrs. A. H., aged thirty-one years; occupation, housework.

Complaint. Stomach trouble for fifteen years off and on; gradually getting worse; until now is unable to eat without distress. Worse symptom is excessive bloating relieved by belching; a sense of smothering with cardiac palpitation. At night must sleep on left side. Epigastric sense of pressure and discomfort; very little nausea; no heart burn; regurgitation of bland fluid; no pain; has lost eleven pounds in the last year and now weighs eighty pounds.

No cough; no sputum; no night sweats; very nervous; has headaches; is easily fatigued and has attacks of dizziness; regular in habits of eating. Bowels are constipated, scybalous, with intermittent diarrhea.

Past Medical History. Unimportant, except for tendency to anemia (simple).

Physical Examination. Fairly well nourished and developed little woman, perhaps five feet tall. Hair, eyes, ears, nose, mouth negative. Color good. Visible mucous membranes very slightly pale. Complete absence of nails on both thumbs and both index fingers, which she states is congenital, and has appeared in each generation for several generations. Chest well formed; symmetrical. Lungs negative, except for moderate dulness at both posterior apices. Heart negative. Abdomen: liver dulness normal in extent; spleen and kidneys not palpable. Stomach normal in position, somewhat dilated, particularly to the left. Knee-jerks exaggerated.



	10	20	30	40	50	60	70	85
FREE HCL.	0	0	0	0	0	0	0	0.
TOTAL ACIDITY	2	5	5	11	15	13	10	10

CHART I.—H. M., Case IV. December 22, 1914. Cancer of stomach. Total chemical achylia; malignant. Wolff-Junghans reaction positive. Occult blood, + +.

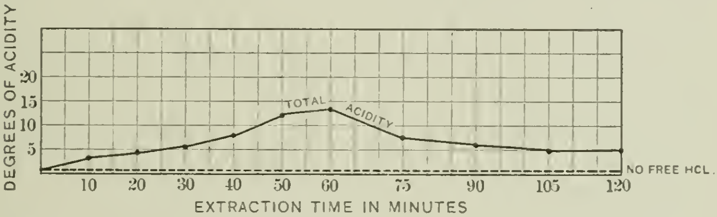
Blood Count: Red-blood cells, 5,104,000; hemoglobin, 88 per cent.; color index, 0.8; white-blood cells, 6,000. Differential count: Polymorphonuclear neutrophics, 60 per cent.; transitionals, 34 per cent.; lymphocytes, 32 per cent.; large mononuclears, 4 per cent.; total, 100 per cent. No polychromatophilia; no poikilocytosis; no neucleated red cells.

Urinary Analyses: All negative except for low specific gravities, from 1,006 to 1,015.

Examination of stools shows free-fat globules; fatty acid crystals; a few striated muscle fibers; otherwise negative.

Gastric Analyses: A series of gastric analyses (twelve in number) covering a period from July 26, 1912, to August 11, 1915, have all shown a total achylia. No free HCl occurred at any time; a combined HCl on two occasions of 2 and on one occasion 10.4, and total acidities ranging from 6 to 12 after Ewald test meals and on one occasion 15 after a mixed meal. There have never been present either enzymes or proenzymes. There has uniformly been found a considerable amount of intimately mixed mucus. Occult blood reactions in the gastric filtrates have been negative except on one occasion. Starch digestion has been uniformly active, always passing through the erythro- and acroödextrin stages and giving well-marked sugar reactions. The odor has always been bland like that of bread soaked in water. The rate of motility has always been increased. The amounts recovered at sixty minutes from Ewald test meals of 35 gm. of bread and 300 c.c. of water, varying between 15 and 35 c.c. in amount and giving about 50 per cent. of filtrate. Fractional studies, withdrawing small amounts at intervals of ten minutes, have likewise shown a total achylia during the entire digestive cycle (see curve, Chart II).

Gastric Sediments: From time to time flakes of mucous membrane have been recovered, usually showing point of rupture at muscularis mucosæ; marked diminution in glandular elements with gastric tubules showing various stages of atrophic degeneration and a considerable increase in the interglandular connective tissue, with occasional areas of congestion, and at the periphery often showing a layer of mucus (see Fig. 9). The Wolff-Junghans reactions have been negative, showing a demonstrable albumin ring in no dilution above 1 to 20. Under a substitution form of therapy, using fairly large amounts (30 to 60 drops) of dilute hydrochloric acid and essence of pepsin with meals and 5 to 7 grains of pancreatin three hours after meals, the progress of this case has been most satisfactory. She has been encouraged to take a morning cold bath and moderate exercise in the open air, and as much amusement as she wishes. Her diet has been arranged to give the maximum amounts of protein, carbohydrates, and fats to the point of digestive tolerance, and without showing any of these elements in her stool. For practically two years and at present she has been symptomatically cured, notwithstanding the persistent failure in gastric juice. Her weight has been increased, and now fluctuates between sixteen and twenty pounds more than when she first came under observation.



FREE HCL.	0	0	0	0	0	0	0	0	0	0
COMB. HCL.	0	0	0	0	0	0	0	0	0	0
TOTAL ACIDITY	1.5	4	5	8	12	13.5	7	6	5	5
ENZYMES	0	0	0	0	0	0	0	0	0	0
PROENZYMES	0	0	0	0	0	0	0	0	0	0
OCCULT BLOOD	0	0	0	0	0	0	0	0	0	0

CHART II.—Mrs. A. H., Case V. January 12, 1915. Achylia gastrica. Total chemical achylia; benign.

THE INFLUENCE OF ATHLETIC TRAINING ON BLOOD-PRESSURE.

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The present study was undertaken with a view of determining the influence of a specified period of training on the blood-pressure. Because of the availability of material for study, football was taken as the type of athletic training for investigation. The men reporting for varsity and freshman teams are required to receive a permit to train from the medical adviser, and the present blood-pressure study represents merely an enlargement of this routine.

Blood-pressure readings were taken by the auscultatory method preceding and succeeding fifty stationary running steps before and after the football season, and then in May after a period of rest. Uniform hours were selected for all cases to eliminate possible error from diurnal variations. The fifty steps were controlled by commands as to height and rapidity, the steps being completed in twenty-five seconds (MacKenzie). The systolic and the diastolic readings were made with the patient in the sitting posture, with a Faught mercury manometer. The pulse rate was taken by an assistant. Then with the arm band still in place the fifty stationary steps were taken and second readings were made. The method is doubtless open to criticism, but, even though crude, the uniformity of results bespeaks its comparative accuracy.

The data are complete in the main for forty-five athletes completing the football season. The data of sixty-eight men who either failed to complete the season's training or to report at the end of the season are added to render the average of men entering training more general. In addition to the blood-pressure statistics, we will endeavor to show what percentage of athletes start the season with cardiac enlargement, and what proportion develop this condition during their period of training.

A comparison of the blood-pressure and pulse rate before training in both groups A and B shows a close coincidence in systolic, diastolic, and pulse-pressure, and in the pulse rate before and after the test exercise. We may therefore conclude that the complete group B is a fair average of men entering the sport.[1]

For their average age, twenty to twenty-one, the systolic pressure of 118 mm. Hg., and the diastolic pressure of 82 mm. are relatively high. Erlanger gives 100 to 110 mm. for the systolic and 60 to 70 mm. for the diastolic pressure at this age. A series of 20 non-athletic individuals in the University of Wisconsin[2] showed a systolic pressure of 111 mm. and a diastolic pressure of approximately 80 mm. The literature affords no normal reaction to test exercises.

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[1] More complete data will be found in tables in reprint of this article.

In our present study the presence of an increase in the reaction of cardiac activity attendant on slight exertion is noted among athletes out of training as compared with non-athletes. The non-athletes shows only a 32 per cent. increase in cardiac rate on the exertion of fifty stationary steps,[3] whereas the average of the athletic groups is 45 and 44 per cent. It has been our observation that this condition pertains in a large proportion of athletes out of training. Pembrey and Todd[4] noted a similar reaction among men in training as compared with untrained, but offered no explanation.

From Group A the cases showing appreciable cardiac hypertrophy have been separated. Twenty-seven individuals (39 per cent. of the total) have this condition. The blood-pressure of these men coincides closely with the rest of the group.

The results of our observations on men completing their football training are compiled in Table I. For comparison the men are grouped according to increase, decrease, or stationary condition of blood-pressure; the number of individuals and percentages of the total these represent is stated along with change in millimeters of mercury. The pulse, systolic and diastolic phases of blood-pressure are grouped separately both before and after exercise, and in each of the periods, "after the season" is compared with "before season," "after a period of rest" is compared with "before" and "after season." These groups do not correspond to the large groups noted above. The total average increase or decrease for each phase of blood-pressure at each period is represented by the figures at the bottom of the table.

The total averages are probably better studied from the curves shown in Figs. 1 and 2. A normal curve is drawn for the blood-pressure before exercise, but as we have stated previously, no data are available for the normal reaction after exercise.

From Fig. 1 it will be noted that the systolic pressure of the athlete at rest before training averages 8 mm. of mercury higher than the resting non-athlete; the diastolic pressure is, however, 12 mm. higher in the average athlete. Therefore, the pulse-pressure in the resting athlete before the period of training averages 4 mm. less than the non-athlete. After the football training the following interesting condition pertains: The systolic pressure falls 6 mm., or to within 2 mm. of the normal, while the diastolic pressure fails to approach the normal line by 7 mm., not because there is not a fall relative to the systolic fall, but because of previous high diastolic

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[2] Shumacker and Middleton, Jour. Am. Med. Assn., 1914, lxii, 1136.

[3] Ibid.

[4] Jour. Phys., 1908, xxxvii, 66.

TABLE I.—COMPARISON OF BLOOD-PRESSURE IN FOOT-BALL MEN COMPLETING TRAINING SEASON.

		After season compared with before season.						After period of rest compared with: Before season.						After season.					
		Before exercise.			After exercise.			Before exercise.			After exercise.			Before exercise.			After exercise.		
		Systolic.	Diastolic.	Pulse pressure.	Systolic.	Diastolic.	Pulse pressure.	Systolic.	Diastolic.	Pulse pressure.	Systolic.	Diastolic.	Pulse pressure.	Systolic.	Diastolic.	Pulse pressure.	Systolic.	Diastolic.	Pulse pressure.
Group A. Increased	Number of individuals.	11	11	21	14	16	19	28	26	22	22	18	19	35	30	20	24	24	21
	Percentage of total....	24.4	24.4	46.6	32.5	37.2	44.1	73.6	68.4	57.9	59.4	48.6	51.3	92.1	78.9	52.6	63.1	63.1	55.2
	Average in mm of mercury..............	+5.0	+9.0	+6.0	+7.8	+5.7	+12.4	+9.8	+9.2	+7.8	+11.3	+7.5	+11.6	+12.5	+11.4	+7.7	+14.1	+8.5	+12.4
Group B Decreased	Number of individuals.	30	28	21	25	22	21	8	8	13	12	14	12	2	3	12	5	7	13
	Percentage of total....	66.6	62.2	46.6	58.1	51.1	48.8	21.0	21.0	34.2	32.4	37.8	32.4	5.0	7.8	31.5	13.1	18.4	34.2
	Average in mm. of mercury..............	−10.0	−12	−7.3	−12.6	−13.9	−10.8	−5.5	−8.5	−8.6	−10.2	−11.0	−6.5	−13.0	−6.6	−6.2	−6.8	−4.8	−9.6
Group C. Unchanged	Number of individuals.	4	6	3	4	5	3	2	4	3	3	5	6	1	5	6	9	7	4
	Percentage of total....	8.8	13.3	6.6	9.3	11.6	6.9	5.0	10.5	7.8	8.1	13.5	16.2	2.6	13.1	15.7	23.6	18.4	10.5
Total Average	Increase (mm. of Hg.).	..	..		..	..	+1.0	+5.0	+4.0	+1.0	+4.0	+1.0	+3.0	+11.0	+9.0	+2.0	+8.0	+6.0	+2.0
	Decrease (mm. of Hg.).	−6.0	−5.0	−1.0	−4.0	−5.0													

pressure. With cessation of athletic training, both the systolic and diastolic pressures advance not only to, but beyond the ante-season records. This is a proportionate increase, and the pulse-pressure remains practically unaltered.

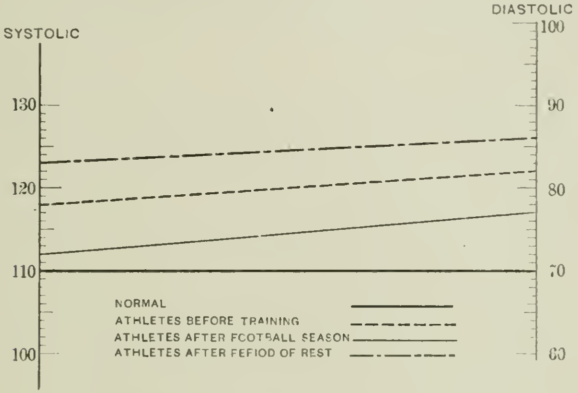

Fig. 1.—Total average blood-pressure in athlete before test exercise.

Fig. 2 indicates that the curves of blood-pressure after exercise follow the same general tendency of the systolic and the diastolic pressures of the resting readings at the corresponding periods. By this we mean that the "before training" curve occupies a position between the "after season" curve below and the "after period of rest" curve above, after exertion as well as in the resting state.

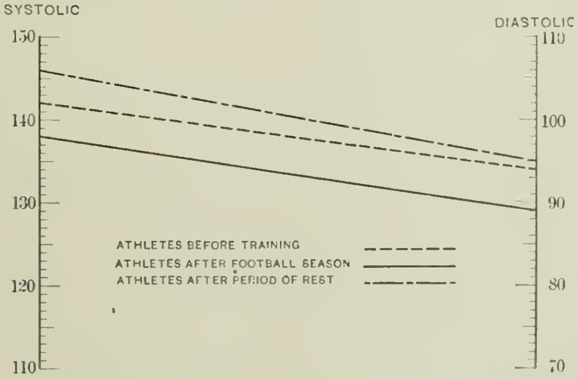

Fig. 2.—Total average blood-pressure in athlete after test exercise.

Of course, the diastolic pressure does not increase proportionately with the systolic pressure on sudden exertion.[5] This phenomenon leads to a marked increase in the pulse-pressure curves after exertion, which, with the increase in pulse rate, is interpreted by Lowsley to mean augmentation with acceleration of cardiac activity. Before training, on exertion, the average systolic pressure increase is 24 mm. Hg., while the average diastolic increase is 12 mm. After their football training the average systolic increase is 26 mm. and the average diastolic 12 mm. After a period of rest the systolic pressure reaction to fifty running steps is 23 mm., while the diastolic increase averages 9 mm.

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[5] Lowsley, Amer. Jour. Phys., 1911, xxvii, 446.

The possible relation between an increase in the skeletal musculature with a corresponding decrease in subcutaneous fat and these blood-pressure changes, *viz.*, the decrease of the systolic and diastolic readings with training, must be considered. Janeway[6] and Hensen[7] reported equal blood-pressure in arms of unequal size, and concluded that soft tissues played no important role in the blood-pressure readings. Von Recklinghausen's observations led him to the conclusion that with an arm band of 12 cm. or wider, soft tissues do not influence the blood-pressure readings. We followed the weight of twenty of the men through their training and found that no general rule could be applied; some men lost weight early in their training, but later regained the loss; some steadily lost while still others gained ground from the outset. There was no tendency on the part of those who lost weight to fall into a group of strikingly low pressure. On the other hand, gain in weight was no index for a rise in blood-pressure. As a matter of fact, while we assume that loss of weight being due to a combustion of subcutaneous and other stored fats to a large degree, and therefore assume that the removal of this tissue from the arms would lessen the resistance to compression, no confirmation could be found for such theory in even our most striking weight changes.[8]

CONCLUSIONS. The effects of a football training period on the blood-pressure are fairly constant, namely:

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[6] Arch. Int. Med., 1909, iii, 474.

[7] Deutsch. Arch. f. klin. Med., 1900, lxxii, 443.

[8] As to cardiac hypertrophy, in Group A, 27 individuals of a total of 68, or 39 per cent., had an enlarged area of cardiac dulness before the training period. In Group B, 28 men out of 45, 62 per cent., showed hypertrophy before training. The discrepancy here is explained by the fact that for the greater part Group A are freshmen, while the majority of Group B are varsity men. After the football season, of 45 men completing their training, 40 had cardiac hypertrophy. Of the 5 men completing the season without cardiac enlargement, our examination in May revealed the fact that 4 of these had developed an appreciable enlargement in the interval, and the fifth had in the meanwhile been forced to withdraw from the University on account of a questionable pulmonary lesion; 3 of the men had, however, engaged in some other sport, making the relation between their football training and cardiac condition questionable. These figures would seem to indicate rather conclusively that cardiac enlargement of a rather moderate degree is the natural consequence of the football training. In addition there is an apparent tendency for the enlargement to the right to disappear, and in certain cases, for the reduction of left-sided enlargement. There can be no question but that these cases represent hypertrophy with moderate dilatation. The failure of the cardiac enlargement to disappear in the five months intervening between the end of football season and our last examination in May seems to be fair proof of the permanency of this condition.

1. A proportionate decrease in both systolic and diastolic blood-pressure during the training period.

2. With a period of rest succeeding the training period, a rise of systolic and diastolic blood-pressure beyond the anteseason records.

3. The blood-pressure reaction to the given test of fifty stationary running steps is scarcely altered by a period of training.

As a basis for explanation for these phenomena several hypotheses may be stated:

(*a*) *Vascular Influence.* The decrease of blood-pressure during training may result from an enlargement of the vessels to the skeletal muscles with lessened peripheral resistance. Or this lessened peripheral resistance may result from a compensatory vasodilatation to accommodate for the increase in cardiac output and work from athletic training. From the vascular stand-point the secondary rise of blood-pressure after a period of rest would be explained by the logical assumption of a return of normal vasomotor tone, which in the presence of a hypertrophied myocardium, or increased cardiac power, would lead to increased blood-pressure from a relative increased peripheral resistance with an accompanying increase in systolic output. Moderate peripheral sclerosis from overstrain would likewise give increased resistance with a tendency to higher blood-pressure than normally existed in a given individual.

(*b*) *Cardiac Influence.* The primary decrease in blood-pressure after a period of training may be the result of a temporary moderate cardiac dilatation. By regaining normal myocardial tone with rest and the development of cardiac hypertrophy the increase of blood-pressure during this period may be explained.

Perhaps both of these factors are active in the production of the phenomena.

THE ADMINISTRATION OF GLUCOSE SOLUTIONS AS A PROPHYLACTIC AGAINST POST-OPERATIVE SHOCK.

By A. C. Burnham, M.D.,
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In a recent article[1] the writer has called attention to the present status of our knowledge of the various methods of parenteral nutrition. From the experimental data cited, it is apparent that, theoretically and practically, an animal may be kept for a considerable period in nitrogen equilibrium and at a constant weight by the intravenous injection of solutions containing amino-acids and glucose (Henrigues and Anderson). The subcutaneous administration of fats is possible, and they are apparently metabolized and supply a portion of caloric need of the organism.

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[1] Parenteral Nutrition and its Surgical Application, Med. Record, July 25, 1914.

For practical purposes, however, of the three main groups of nutritives—fats, proteids, and carbohydrates—only one (carbohydrate in the form of glucose solution) is available for the surgeon in the treatment of those accidents and disagreeable symptoms which may accompany, or occur shortly after, a major operation.

It is the desire, further, to emphasize the value of glucose solutions as a prophylactic against some of the unpleasant post-operative complications, as well as to call attention to the methods of its administration, that has led to the preparation of this article.

It may be stated as a postulate that patients who are well nourished stand operation better than patients who are poorly nourished. This is apparent to all, but the fact that patients are frequently underfed for a period of several days before operation is often regarded as of little moment. A patient who is well nourished has food material stored in his tissues to supply his requirements for a short period. This is principally in the form of glycogen and amino-acids, which are present in the liver and blood, and may be called upon in sudden emergencies. It is not sufficiently appreciated that after the first twenty-four hours these circulating and stored nutritives are largely exhausted, and after that time the body requirements are met almost wholly by the utilization of proteid and fat derived from the patient's own tissues.

It has long been recognized that starvation produces a condition known as acidosis, and that this same condition occurs after several days of a strict carbohydrate-free diet; or, pathologically, in patients suffering from diabetes who are unable to utilize the carbohydrates present in their food. The same condition also occurs in certain types of metabolic disturbances in children, in some cases of vomiting of pregnancy, and frequently after long anesthesia.

Acidosis should be recognized as a condition—not as a definite pathological process—the salient characteristic of which is the excretion of acetone bodies in the urine (and breath) and a marked increase in the titrable acid in the urine. It is commonly supposed that there is a condition of diminished alkalinity in the blood, but this statement has been challenged, the assertion being made that the blood is always neutral, and consequently a diminished alkalinity is impossible in that it is incompatible with life. The determination of the reaction of the blood is fortunately not essential for the comprehension of the clinical importance of acidosis. Whether the blood be acid, or alkaline, or neutral, there is in this condition a great decrease in available alkalies, and this, carried to the extreme, always ends in coma and death. Emerson has characterized the condition as "alkali starvation."

In the management of those diseases which are commonly classified as surgical, there are two conditions which are recognized as giving rise to acid intoxications, or acidosis. The most common type is that following anesthesia, which occurs to an appreciable degree after from 30 to 60 per cent. of all anesthesias. The acidosis following starvation, as it occurs in those diseases associated with the inability to retain nourishment because of persistent vomiting, is not uncommon among surgical patients, and when it occurs is considerably less amenable to treatment than the uncomplicated post-anesthetic acidosis. The acid intoxication following both of these factors acting together has been found to be much more severe than that following either acting alone. That this is true is shown both by laboratory experiments and clinical experience. Experimental evidence points to starvation as the predominant factor in acidosis following prolonged vomiting, while, as was shown by Waldvogel, the toxic action of the anesthetic had an important influence in the production of post-anesthetic acidosis. Furthermore, it has been definitely proved that acidosis may be prevented or markedly diminished by the administration of carbohydrate food. The symptoms may be relieved by the use of alkalies, but the underlying disturbance is overcome only when sufficient carbohydrate food may be absorbed and oxidized to prevent the excessive metabolism of fats and proteids.

The effect of diet upon animals poisoned with chloroform was shown by the experiments of Opie and Alford in 1914.[2] If the conditions in the human body are comparable to those in animals, and there is every reason to believe that in this respect they are the same, then this work of Opie and Alford is of the utmost importance to every surgeon, and the inference which they draw as regards diet deserves far greater application than it has yet attained.

Animals (white rats) were fed for six days upon diets which consisted solely of either fat, proteid, or carbohydrate, and at the end of that time were given what was presumably the minimum fatal dose of chloroform injected beneath the skin. The results as given by Opie and Alford are shown in the following table:

LENGTH OF LIFE OF ANIMALS IN DAYS AFTER RECEIVING SPECIAL DIET FOR SIX DAYS.

Chloroform per 100 gm.	Diet: oats and sugar.	Diet: meat.	Diet: fat.
0.025	....	.....	L
0.05	L	11	3
0.1	10	L	1
0.15	L	L	1
0.2	L	3	2
0.25	L	3	2
Average duration of life	10+	$5\frac{2}{3}$+	$1\frac{1}{5}$

L = Lived.

From the above experiments, and others in which the results were confirmatory, Opie and Alford draw the following conclusion: "The experiments furnish evidence that fat administered to animals and presumably stored in the liver increases the susceptibility of the organ to the injurious action of chloroform. In view of the well-known solubility and diffusibility of chloroform in fats, they suggest that the fat of the liver cell determines the fixation of chloroform and occurrence of necrosis. The experiments with carbohydrates, on the contrary, furnish confirmation of the views of those who maintain that carbohydrates protect the body proteins from disintegration."

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[2] The Influence of Diet on Hepatic Necrosis and Toxicity of Chloroform, Jour. Amer. Med. Assoc., 1914, lxii, 895.

In the light of these experiments, as well as those of Waldvogel, it is important that patients about to be subjected to major surgical operations should, when possible, be put through a course of forced carbohydrate feeding for a short period immediately preceding the operation, and should receive carbohydrates in an available form soon after operation.

Secretan has called attention to the importance of giving food shortly before anesthesia as a prophylactic measure against post-operative shock. He asserts that it is usually safe to give some easily digested food from two to four hours before the anesthesia is begun. A patient in whom there is no contra-indication to oral feeding may be given a meal containing a considerable quantity of carbohydrate food in the shape of bread or cereal eight to twelve hours before operation, and a feeding which contains 100 to 200 calories in the shape of easily absorbable carbohydrate about three hours before the anesthesia is begun. In practice I have found that the latter is best accomplished by giving either six ounces of coffee or orangeade to which has been added one ounce of lactose. The above procedure should assure the organism of a considerable store of readily available glycogen during the period of anesthesia.

If we grant the plausibility of the argument up to this point it must necessarily follow that carbohydrate feeding should be instituted at the earliest opportunity after the operation. During the anesthesia, and for a period afterward, varying from a few hours to a few days in individual cases, oral feeding is impossible, so that we are, of necessity, forced to resort either to subcutaneous or rectal nutrition, or both. In the paper to which reference is made at the beginning of this article, the writer has discussed the various types of nutritives which theoretically may be used for subcutaneous nutrition, the conclusion being reached that glucose is the only form of nutritive which is clinically available for this purpose. Barlow recommended the subcutaneous use of glucose in 1895, and it has been in sporadic usage since that time; but it was not placed upon a scientific basis in surgical cases until the publication of Kausch, in 1911.

Sugar, in the form of glucose solutions, supplies energy to the cells and aids in tissue repair; it diminishes acidosis and thus tends to remove one of the factors in the cause of post-operative vomiting; it neutralizes certain poisons in the circulation (the conjugate glycuronates is the best example of this action); and it is possible that it acts as a direct cardiac stimulant and food.[3] In addition to this, the solution introduced has many of the advantages and few of the disadvantages of saline solutions. Only a small percentage of the glucose injected hypodermically finds its way into the urine (usually from 2 to 5 per cent.). The remainder, as has been proved by the calorimetric experiments of Vezar and von Fejer,[4] is burned in the body, causing an increase in heat formation and a corresponding increase in the respiratory quotient.

Kausch[5] recommended 7 per cent. solutions intravenously and 4 to 5 per cent. solutions by hypodermoclysis. Solutions should be freshly prepared and sterilized, as they become more easily contaminated than does the ordinary saline. Strictly speaking, contamination is as easy in one as in the other, but owing to the fact that glucose is an excellent culture medium, accidental contamination is of more consequence than it is in common salt solution. Following the use of glucose by hypodermoclysis, there is no more pain or discomfort than after the injection of physiological salt solution. As much as two or three liters, representing from 90 to 210 grams of glucose, may be given during twenty-four hours, the amount depending on the character of the case and the urgency of the symptoms.

In addition to the hypodermic administration, glucose may be given by proctoclysis during anesthesia and for a period of several days after operation. It is given in 5 per cent. solution, dissolved in ordinary tap water, 12 to 16 ounces being introduced during the operation, and its administration continued, by the Murphy drip method, after the patient has returned to the ward. This method is so simple and has apparently been of such value that it should be used as routine after every severe major operation. From 300 to 500 calories a day may be introduced by one or both of the above methods without discomfort to the patient. This quantity, while insufficient to supply all the total energy requirement, is of great importance in the prevention of excessive nitrogen waste.

Three typical cases may be cited to illustrate the method of using glucose in routine practice.

Case I.—Male, aged twenty-four years. Well nourished. Operation for inguinal hernia. Sac adherent and operation prolonged. Twelve ounces of 5 per cent. glucose given by rectum as soon as patient returned to ward. Good recovery. Very little vomiting.

Case II.—Female, aged thirty-one years. Fairly well nourished. Acute appendicitis. Local peritonitis. Pulse rapid. Sixteen ounces of 5 per cent. glucose by rectum during closure of wound. Murphy drip, 5 per cent. glucose begun one hour after returning to ward. Good recovery. Very little vomiting.

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[3] Gigon and Massini have brought forth arguments based upon laboratory findings which tend to prove that isolated muscle contains an enzyme by which it is enabled to utilize sugar directly, Biochem. Ztschr., 1913, lv, 189.

[4] Biochem. Ztschr., 1913, lii, 140. [5] Deutsch. med. Wchnschr., 1911, xxxii, S.

Case III.—Female, aged thirty-seven years. Poorly nourished. Pulse rapid. Removal of large ovarian cyst. Hypodermoclysis of four pints of 4 per cent. glucose during operation. Murphy drip, 5 per cent. solution after operation. Slow recovery.

In the above three cases glucose solutions were given simply as a routine procedure without regard to urinary findings or other symptoms of acidosis. In other words, it was given to those cases in which saline solution is ordinarily used as a prophylactic against post-operative shock.

Patients in whom a condition of acidosis may be suspected, should have a complete urinary analysis before operation, and if acetone be found, measures taken to diminish this condition as much as possible before operation is attempted. It should be remembered that these patients are poor surgical risks, and that, except in the most urgent cases, it is necessary to take measures to increase the available supply of fixed bases. This may be accomplished in two ways, namely, the administration of alkalies or of carbohydrates.

No attempt is made here to outline the complete treatment of acidosis, but it may be stated that it is customary to give an alkali in the shape of bicarbonate of soda until the urine becomes neutral. This will usually require much larger doses than are customarily given. Occasionally as high as 50 to 100 grams of sodium bicarbonate must be given before the reaction of the urine becomes neutral or alkaline.

In order to diminish the formation of acid bodies, large amounts of carbohydrate should be given, and it is exactly in those cases in which the administration of carbohydrates by mouth is impossible that the subcutaneous and rectal injections of glucose solutions find their indications.

The common conditions associated with acidosis are diabetes, nephritis, diseases of the liver, and after protracted vomiting. It is the last of these conditions that is seen most frequently by the surgeon and in which the administration of glucose plays its most important role.

Following operation, especially in the so-called "delayed chloroform poisoning," and in some cases which, for some reason, do not permit of oral alimentation, the urine should be carefully watched and at the first indication of acidosis, glucose solution and alkalies should be given either by mouth or rectum or directly into the circulation.

To recapitulate: (1) Glucose solution should be given as routine after every operation in which we have reason to fear more than the ordinary amount of post-anesthetic shock; (2) it should be given as routine in every case where post-operative oral feeding may be difficult or insufficient for a considerable period after operation; (3) it should be given as an emergency measure either before or after operation for the relief of an existing or threatened acidosis.

REVIEWS

Outlines of Internal Medicine. For the Use of Nurses. By Clifford Bailey Farr, A.M., M.D., Instructor in Medicine, University of Pennsylvania; Assistant Visiting Physician, Philadelphia General Hospital; Pathologist to the Presbyterian Hospital. Pp. 408; illustrated with 71 engravings and 5 plates. Philadelphia and New York: Lea & Febiger, 1915.

The introduction of systematic courses in internal medicine in those hospitals which offer thorough theoretical as well as practical training to their nursing staff has made necessary the employment of a text-book upon the subject, which will deal briefly but comprehensively with internal medicine in all its important phases. To meet this need the present volume has been written, and, after a careful perusal of it, the reviewer feels that the need has been well met. The book has been carefully prepared; the essentials have been included, and the non-essentials have been omitted, so that persons desiring a knowledge of the rudiments of internal medicine may read with the assurance that what they read is of importance, that nothing of importance has been left out in the description of the individual diseases, and that if they remember what they read they will have a fitting frame-work, upon which to hang the prints of deeper, more elaborate study, when essayed.

The work is divided into ten parts, dealing respectively with the diseases of the various systems, the disorders of metabolism, the diseases due to physical causes and poisons, and the diseases due to animal or vegetable parasitic causes. Each part is preceded by a section dealing with general considerations and symptomatology of the diseases peculiar to the system under consideration. This is an especially valuable addition to the book, because it smoothes out the way for the beginner before she enters upon the rough road that leads to the knowledge of the special diseases. Each of these, in turn, is treated under the subheads of symptoms and treatment while the more frequent and more important diseases also have subheads of causes, course, complications and prognosis. In this way practically nothing is forgotten or omitted that is likely to be of importance to the future graduate nurse.

But few criticisms may be made of the book; it might seem well to omit nearly all references to physical signs, to delimit drug therapy to general terms, and to cut out entirely case reports or case illustrations. Typhus fever, incidentally, should be more properly grouped under the diseases disseminated by body lice than those carried by ticks, as the latter animal's habitat is the country, while its cousin, the louse, is found where men congregate together in large numbers. Taking it all in all, however, the book stands as a careful, conservative, practical, abbreviated, treatise upon an extremely important subject. J. H. M., Jr.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics, Materia Medica, and Diagnosis in the Jefferson Medical College; Physician to the Jefferson Medical College Hospital, Philadelphia, etc.; assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia, etc. Vol. I. March, pp. 382; 15 illustrations. Vol. II. June, pp. 445; 100 illustrations. Philadelphia and New York: Lea and Febiger, 1915.

WITH the March number appears the first of the volumes of *Progressive Medicine* for this year. The contents of this volume embrace a wide range of subjects of unusual interest. The general surgical section consists of an article on the surgery of the head and neck by Charles H. Frazier, than whom there is no one better qualified to deal with these subjects of ever-increasing surgical importance, and one on the surgery of the thorax, a topic of great present-day interest, written in his usual scholarly manner by George P. Müller. The enormous amount of work constantly in progress on the infectious diseases is strikingly brought out by John Ruhräh in an admirable contribution of 145 pages, which embraces almost the entire range of the acute infections. In an article of about 25 pages, Floyd M. Crandall points out the important advances that have been made of late in pediatrics, particularly emphasizing diseases of the heart in children, acidosis in infancy, and recurrent sibilant bronchitis. In an exceedingly painstaking and thorough manner George B. Wood discusses recent contributions to rhinology and larynology. As is but proper, the accessory sinuses of the nose and the tonsillar tissues claim a large share of his attention. Truman Lawrence Saunders reviews the problems of otology with nice critical judgment, thereby furnishing a most instructive concluding article for this excellent volume.

The June issue of *Progressive Medicine* is always one of the most interesting and important volumes of the year. With the subject of hernia discussed in all its varied phases by William B. Coley; with the ever-increasing problems of the surgery of the abdomen dwelt upon in all their many details by such a critic as John C. A. Gerster; and finally with an authority of such prominence as John G. Clark emphasizing the advances in gynecology that have occurred during the past year, it is small wonder that the first half of this volume offers the reader a wealth of surgical information that is indispensable. From the medical stand-point the volume is of no less interest, thanks to the usual able contribution by Alfred Stengel, who first reviews diseases of the blood, particularly leukemia and pernicious anemia, then takes up the absorbing subject of diseases of the thyroid and other ductless glands, and concludes with a discussion of diabetes, gout, and scurvy. Edward Jackson's concise but well-written review of ophthalmological advances is the concluding contribution to this really noteworthy volume. G. M. P.

THE ORIGIN AND NATURE OF THE EMOTIONS. By GEORGE W. CRILE, M.D. Philadelphia and London: W. B. Saunders Company, 1915.

THE reviewer has found this well-printed book difficult to review. The views therein presented are extremely speculative, and at times so arbitrarily verbal that the reviewer has not always felt certain that the author really means what he says. Dr. Crile lays stress upon certain histological appearances described as occurring in cells of the central nervous system under conditions of disease, fatigue and experimentation. In the interpretation of these findings he makes free use of the modern concepts of internal secretion of the several ductless organs, associating them in a schematic relationship to the brain, liver, and muscular system. By means of these speculations, supported by experiments that often do not bear upon the actual question at all or permit of several interpretations, hypotheses are erected purporting to explain about everything in the domains of psychology, physiology, and pathology. The histologic changes described in the cells of the central nervous system are not commonly regarded as possessing the unequivocal quality that is here ascribed to them. The reviewer has been advised by competent neurohistologists that the methods, results and interpretations are, to say the least, still under discussion. Concerning the influences of the internal secretions of the ductless glands, the literature is today in a state of extreme confusion and contradiction, and upon the published data one could erect several incompatible systems and not be able to prove or disprove any of them. Dr. Crile generally avoids discussion of the conceptions of other workers in this field; he selects from the mass what suits his hypothesis and leaves the rest without comment. In fact, naivety is one of the characteristics of the book, previous work of competent investigators being often entirely overlooked and statements of familiar biological fact uttered as though they were original promulgations. Anyone who feels that this stricture is too severe is requested to make the following test: The chapter entitled "A Mechanist View of Psychology" is first to be read. After this are to be read the following, bearing in different ways upon the problem: Loeb, "Mechanistic Conception of Life" (tropisms are not discussed by Dr. Crile); Mach, "The Analysis of Sensations;" Singer, "The Pulse of Life" (*Journal of Philosophy, Psychology, and Scientific Methods*, xi, 645); and Bertrand Russell, "Our Knowledge of the External World." Following this the chapter on the "Mechanistic View of Psychology" is to be re-read. The result will be illuminating. Possibly it was with the work of Loeb (and other workers in comparative psychology), in mind that Dr. Crile expressed the hope that "we dispossess ourselves of the shackles of psychology." The extreme discursiveness of the presentation cannot fail to impress the critical reader unfavorably. If the opinions expressed in the mechanistic view of psychology are correct, the systematic psychologists of all schools are, for the largest part, in the wrong, including Spencer and Bergson, who owe so much to the theory of evolution. It is, of course, possible that this is true; but judged by the evidence presented in this book, it is highly improbable. The familiar German expression, Wer Vieles bringt wird Jedem Etwas beingen, seems here to have been paraphrased to the effect that if one attempts to explain everything one is sure to explain something.

The statement that "love is a phylogenetic conjugation without physical action" deserves literary immortality, and indicates that Freud has overlooked something. A futurist definition of humor is contained in the following: "A common example of the same nature is that encountered on the street when a pedestrian slips on a banana peel, and, just as he is about to tumble, recovers his equilibrium. The onlookers secure relief from the integration to run to his aid by laughing. On the other hand, should the same pedestrian fall and fracture his skull, the motor integration of the onlookers would be consumed by rendering physical assistance; hence there would be no laughter." One wonders what would be the physiological situation of the onlooker who, in the event of the man not falling, finds nothing to laugh at? On page 131 the statement is made that the victim of a high-speed bullet feels no pain because his remote ancestors had not developed response to fast-moving stimuli. "There was no weapon in the prehistoric ages which could move at the speed of a bullet from the modern rifle, therefore, while slow penetration of the tissues produces great pain and muscular response, there is no response to the swiftly moving bullet." While this realization is doubtless a source of great comfort to the unfortunate men now charging trenches in Europe, mingled with feelings of pity for their descendents who may not be thus insensible, one wonders why fear alone is invoked to explain the lack of pain in Livingstone while struggling with a lion; why might not this also have been due to the fact that his prehistoric ancestors had not struggled with lions? In each instance one of several possible variables has been arbitrarily selected, and this in the face of the fact that any form of mental preoccupation, or stress of excitement, may expell the sense of pain from consciousness. The psychology of color sensation is disposed of in the following business-like fashion: "For example, each variation in speed of the light-producing waves of ether causes a specific reaction in the brain. For one speed of ether waves the reaction is the preception of the color blue; for another, yellow; for another, violet." In what the reaction consists is apparently an immaterial detail. In discussing the relations of the outpour of emotions to "phylogenetic experience" (there are here and there in this chapter expressions that remind one of Gertrude Stein) is the following: "The emotions, then, are the preparations for phylogenetic activities. If the activities are consumed, the fuel—glycogen—and the activating secretions from the thyroid, the adrenals, the hypophysis are consumed. In the activation without action, these products must be eliminated as waste products, and so a heavy strain is put upon the organs of elimination." Where has it been shown that the products of the ductless organs are eliminated after the fashion of urea, or that this elimination is a heavy strain? The problem of consciousness—unsolved from Socrates to Royce—is elucidated in the following statement: "We have shown that the effects upon the body mechanism of the action of the various ceptors is in relation to the response made by the *brain* to the stimuli received." "What is this power of response on the part of the brain but consciousness?" The most absolute mechanist can ask for nothing more positive than the following: "If our premises are sustained, then we can recognize in man no will, no ego, no possibility for spontaneous action, for every action must be a response to the stimuli of contact or distant ceptors, or to their recall through associative memory." A purely mechanistic conception, truly (a cross between evolution and internal secretion); but there will still remain considerable difference of opinion concerning the details of the *modus operandi*. Contrasted with the phylogeny of Dr. Crile, the *deus ex machina* of the eighteenth century was a tyro. In another place Dr. Crile selects his company as follows: "Such is the stimulating force of tradition that many who have been educated under the tenets of traditional beliefs will oppose these hypotheses—even violently it may be. So they have opposed them; so they opposed Darwin; so they have opposed all new and apparently revolutionary doctrines." In view of the rather shabby treatment accorded to the Darwinian theory of natural selection at the Darwin aniversary dinner a few years ago, the friends of Darwin will feel glad that he has been rediscovered, though they may object to the crude and arbitrary manner in which the doctrine of evolution is applied to physiology and psychology.

Dr. Crile's views on fever are in some points contrary to the data of the literature, in other respects hypothetical and unproved. "Fever invariably and chills, often, accompany the course of the infections." This statement is simply incorrect. "We must infer, therefore, that the fever is an adaptation on the part of the host for dispatching the enemy," is stated with reference to the work of Bass in the study of the malarial parasite. Bass, in his recent lectures on malaria in Philadelphia, did not interpret the fever as a combatative measure, but rather as the result of the liberation of metabolic products upon the part of the parasites. "Bacteriology has taught us that both heat and cold are fatal to pathogenic infections." Naturally a certain degree of heat is fatal. But there is no adequate warrant for the statement made that "Bacteriologists have taught us that bacteria grow best at the normal temperature of the body, hence fever must interfere with bacterial growth." For a few germs it has been shown that under the abnormal conditions of growth in the culture tube, growth is more rapid at 37° than at 40°. But there is no demonstration that in the infected body, bacteria grow less well at 40° than at 37°. "In fever, then, we have diminished intake of energy (or may have) but an increased output of energy —reviewer; hence the available potential energy of the body is rapidly consumed." In this book, as elsewhere, Dr. Crile confuses increase of body temperature with increase of heat production, apparently regarding the terms as synonymous, in the sense that increased heat production always accompanies fever. This convenient, though erroneous, assumption has led Dr. Crile in his researches to replace the measurement of heat (by direct or indirect calorimetry) by the simple use of the clinical thermometer. No consideration is given to the point of view, now under investigation, that fever may accelerate the formation of antibodies, using the term in its general sense. One is surprised to read so much of the body reactions to infections without references to immunology.

Unusual stress is laid upon considerations relating to acidity in the body, since "one would expect, *prima facie,* that the normal reaction would be altered by kinetic activation." A list of natural and experimental conditions are named in which it is asserted that the concentration of the hydrogen ions in the blood is increased beyond the range of normal variation. The experimental states described may nearly all be regarded as physiological dissolution. Indeed, Dr. Crile asks whether we may not regard acidosis as the actual final cause of death. No figures are given, no methods described, these being reserved for a future publication. The chapter devoted to this subject opens as follows: "Alkalis and bases compose the greater part of the food of man and animals, the blood in both man and animals under normal conditions being slightly alkaline or rather potentially alkaline; that is, although in circulating blood the concentration of the OH-ions—upon which the degree of alkalinity depends—is but little more than in distilled water, yet blood has the power of neutralizing a considerable amount of acid (Starling, Wells)." Henderson, who should have been quoted in this connection, would give an accurate and much more lucid definition, without the totally meaningless statement that "alkalis and bases compose the greater part of the food of man and animals." With all that is now known of the relations of phosphate and carbonate to the neutralization of acid, of the basic and acid capacities of the blood and tissues and the relations of the concentration of the hydrogen ion to these factors as variables, only confusion is introduced by such a statement as "since at the point of death the blood is always acid, we may infer that some mechanism or mechanisms of the body were evolved for the purpose of changing bases into acids that thus energy might be liberated." Dr. Crile even speaks of the minute alkalinity of adrenalin as being of therapeutic importance. A study of the data bearing upon acid production in the body indicates that there are three degrees or stages in acid production; in the first, the acid formed in the body is neutralized by available labile cations and ammonia, with normal reaction of the blood; in the second, the body yields fixed cations, ammonia and sodium from the bicarbonate of the blood, with normal reaction maintained; in the third, the production of acid is in excess of maximum, chemically available cations, and the hydrogen ion concentration of the blood is increased. These stages naturally merge; the first is of physiological occurrence; the second is common in disease; the third stage has been very rarely observed outside of the state of dissolution. Acid production in the body is, therefore, not a qualitative but a quantitative process. Within the last ten years many estimations of the concentration of hydrogen ions in the blood have been carried out by measurement of the electromotive potential. There are two as yet unsolved methodic problems connected with the technical procedure, and one is not yet in the position of drawing fine distinctions, since the results are not yet reproducible to within one or even two millivolts. The existing data, in figures, indicate that outside of the state of dissolution, appreciable increase in the concentration of hydrogen ions in the blood and tissues is very rare. Many cases of diabetic and uremic coma, stated by Dr. Crile to present demonstrable acidity as their essential abnormality, have been determined to present values lying within normal ranges. Normal figures have been found also in exophthalmic goitre. In a few instances of terminal diabetic coma, just before death, in profound narcosis, and in extreme stagnation of carbon dioxide, slight but demonstrable increase in concentration of hydrogen ions has been observed. Allowance may also be made for the occurrence, especially in young children, of sudden flooding of the body with acid, since the metabolism of the child seems to possess a power of neutralization more limited than in the adult, relatively and absolutely. But beyond this, the statements made by Dr. Crile of the widespread occurance of demonstrable acidity are not borne out by the measurements in the literature, measurements carried out by numerous workers trained in physicochemical research. In the discussion of diabetic acidosis no mention is made of the ketonic acids; diabetic acidosis is lumped with the others. Standing upon the hypothesis that acidosis is the cause of anesthesia both induced and natural in the state of coma of disease, he states that "a reason is supplied for the use of intravenous infusions of sodium bicarbonate to overcome the coma of diabetes and uremia." The numerous physicians who, following the advice of the Naunyn school, have used alkali in the treatment of diabetic coma on the assumption that the ketonic acids formed in this disease were being combined with cation and the body spared its cations, will now feel grateful that a reason for this procedure has finally been discovered. Why alkali should be necessary at all, however, still remains unclear, for we are informed that "water, like air, neutralizes acids." That uremic and diabetic coma should thus be classed together, with our present knowledge of the relation of ketonic acids to diabetic coma and our complete ignorance of the chemical cause of uremic coma, is little less than amazing. Extreme variations of behavior seem to be exhibited by acidosis within the confines of the relatively small state of Ohio. In Cleveland, acidosis causes anesthesia; in Cincinnati, acidosis causes edema. And under the circumstances, one would naturally expect in this book some reference to the work of Fischer.

In every chapter of the book the boundless enthusiasm and engaging personality of the author are in evidence. The reader must be critical, because the author is uncritical. The attempt to expound physiology and psychology phylogenetically is not new. This particular method of attempting the demonstration is individual to the author. The reviewer does not presume to suggest that demonstration may not in future be effected; he is certain that it is not accomplished by the data and hypotheses presented in this book. The words of Russell, applied (unjustly in the opinion of the reviewer) to evolutionism as a total movement, apply to Dr. Crile's evolutionism of the emotions: "Evolutionism is rather to be regarded as a hasty generalization from certain rather special facts, accompanied by dogmatic rejection of all attempts at analysis, and inspired by interests which are practical rather than theoretical."

A. E. T.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF
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Leukocytosis in Dementia Precox.—Zimmerman (*Ztschr. f. d. ges. Neur. u. Psych.*, 1914, xxii, No. 3) made examinations on 50 cases of dementia precox in various stages of the disease. In 96 counts there was leukopenia 41 times and an increase in the white cells 46 times. Normal values were seen in only 9 or 10 per cent. Quantitatively the findings point to an increase in the mononuclear elements generally at the expense of the neutrophilic cells. The eosinophiles may reach 10 per cent. or over and the large mononuclears 11 to 15 per cent. Monocuclear elements are frequently 30 to 40 per cent., and even reached 60 per cent. In one instance the formula was: small mononuclears, 71 per cent.; large mononuclears, 5 per cent.; polymorphonuclears, 22 per cent. With a relative leukocytosis there is always a lymphocytosis. This was absent in only one instance. Generally the increase in small lymphocytes is not very much over the normal, but may be marked. In two-thirds of the cases there was pronounced eosinophilia and occasionally a moderate basophilia. In any case the lymphocytes, large mononuclears, and eosinophiles show little variation, while the total white count may vary a great deal. These findings are of no prognostic value. Eosinophilia was most marked in cases showing outspoken dementia.

Newer Protein Reactions in Spinal Fluid: Their Value and Relation to Antibody Content.—Kafka and Rautenberg (*Ztschr. f. d. ges. Neur. u. Psych.*, 1914, xxii, 4–5), using sufficiently high serum titre, found in spinal fluid of general paretics hemolytic amboceptor for sheep's red cells in dilutions of $\frac{1}{200}$ to $\frac{1}{12}$, independent of the globulin reaction, total proteins, and cell increase. These are only found in cases of cerebral lues when there are meningitic symptoms as shown by cell increase, increase in total proteins, globulin fraction, complement content, and coagulability. As in acute meningitis the amboceptor goes away as the inflammatory process subsides. There exists no marked parallelism between protein and hemolysin reactions. Kafka and Rautenberg represent these by a numeral in which the numerator indicates the antibody value, the denominator the strength of Phase I or the total proteids. In general paresis the number is greater than 1. In fluids from cases of general paresis a clouding occurs even at 30 per cent. saturation with ammonium sulphate, and in cases of acute meningitis a similar result occurs with 28 per cent. This protein fraction bears some relation to the amboceptor content. Quantitative proteins were determined with Nissl's method. Kafka and Rautenberg consider that Phase I offers the best guide to the influence of treatment.

The Action of Various Lipoids Isolated from the Endocrine Glands.—Iscovesco (*Comp. rend. de l. Soc. d. Biol.*, 1913–14, lxxv and lxxvi). *Ovaries:* The lipoid found in ovarian tissue is the same in all animals and possesses the property of stimulating the ovaries and especially the uterus, and calling forth their hypertrophy. This lipoid, moreover, stimulates the thyroid, and has some regulating influence and hastening actions upon the growth of young individuals. *Testes:* Dogs were injected every other day in the cervical region with a lipoid made from testes. Such injections excite the testes very markedly, probably through centres in the spinal cord; the thyroid and kidneys are weakly stimulated. It stimulates growth in young animals while grown ones increase considerably in weight. Similar results are seen in man when given 2 c.c. of the lipoid subcutaneously every day. *Adrenal Cortex:* Lipoids from the cortex stimulate the medulla of the gland markedly, the liver and kidneys very little. It has a strong irritating action upon the skin; in man it causes tachycardia and hyperhidrosis; daily injections of small amounts increase the general condition. *Adrenal Medulla:* This lipoid shows properties very different from those of the cortex. It is a mild stimulant to the adrenal and heart. Daily injections in man cause bradycardia and increased blood pressure. It makes the individual feel remarkably well and ready for work. From these observations Iscovesco thinks that in Addison's disease the asthenia, cardiac and vascular symptoms are due to medullary changes and the pigmentation results from primary or secondary changes in the cortex.

Biological Studies on Eosinophilia.—This report of Weinberg and Séguin (*Ann. de l'Inst. Pasteur*, 1914, xxiii, 470) deals with the production of local eosinophilia by means of eosinophilotactic substances, given to untreated and immunized animals, as well as the relationship between local and blood eosinophilia and anaphylaxis. "Local eosinophilia" was studied in the lids of horses after a few drops of the body fluid of Ascaris megalocephala had been instilled into the eye. Following this, resection of the lids occurred at intervals of from a quarter of an hour to ninety-six hours, and this material was studied histologically. Eosinophiles are found out in the connective tissues of the conjunctivæ as soon as a half an hour after the instillation and at this time the capillaries are filled with polynuclear cells of all kinds. The chemotaxis for the eosinophiles disappears rapidly. The degree of the local eosinophilia is due not merely to the reagent employed, but depends as well upon the eosinophilic content of the animals' blood. Thus, if the latter is low, the local reaction consists solely of an outpouring of neutrophilic leukocytes. There are no substances as yet known which are purely chemotatic for eosinophiles. Similar changes were observed in guinea-pigs injected subcutaneously or intraperitoneally with the fluid from hydatid cysts, or the watery extract of sclerostoma. Of 150 pigs only 7 failed to show eosinophilia following intraperitoneal injection. Guinea-pigs given two or more injections show an increased chemotaxis as a result of this immunization, and numerous eosinophiles can be found in the peritoneal exudate of such animals, tending to show that there is developed a genuine specific reaction to the substance injected, since these animals react, as do normal ones, to the injection of chemotatic substances other than those used for immunization. It can be shown clearly that local eosinophilia occurs at the expense of the eosinophilic content of the circulating blood; the decrease in the blood is most pronounced in immune animals. Pulmonary eosinophilia, which is regarded by some as a characteristic injury in anaphylaxis, occurs normally in most guinea-pigs with well developed blood eosinophilia. The rise that occurs in sensitized animals is not the result of anaphylaxis, but is due to the direct action of the antigen upon the blood-forming centres, which have been sensitized by the primary injection.

Paroxysmal Tachycardia.—Duhot and Boez (*Province méd.*, 1914, xxvii, 260) deal with the history, illness, and autopsy findings in two cases of paroxysmal tachycardia. One came under treatment by reason of numerous short attacks, the other by reason of anginal seizures. A full discussion of the condition is given as well as the theories of its causation. The original view that it is a purely nervous phenomenon is now replaced by the conception of the disease as being a purely cardiac one. The patients characteristically complain of something being out of order in the breast, and this occurs in association with a pulse rate of about 200, an embryonic rhythm, and a fall in blood-pressure. During the seizures one may observe oliguria, albuminuria, and even glycosuria. There are usually present pallor, hyperhidrosis, vomiting, and anisocoria. Very often marked dilatation of the heart occurs during the attack, which may last a few minutes or persist over a week. Suddenly the heart returns to its normal rate, though frequently there are extrasystoles for a while. Once in a while the attack may set in and end in a slow manner. The frequency of the attacks is extremely variable. Duhot and Boez describe three forms: (1) the abortive; (2) a type characterized by long periods of remission; and (3) a progressive type. They consider the prognosis bad in the last two forms. Of etiological moment are diseases of the heart, heredity and a neuropathic constitution, while the exciting factors of the attacks are many, such as psychic traumata, dreams, overexertion, digestive upsets, the onset of puberty, menopause, etc. Infections play a role, and especially rheumatic fever. The nervous system has been held accountable, first by a paralysis of the vagus, then by some process involving the cardiac centre and finally by assuming an undue stimulation of the accelerator nerves. Electrocardiograms show that the excitation does not arise in the node of Keith and Flack, but from an intermediate point in the auriculoventricular system; hence the disorder is a functional one of the primitive bundle, section or compression of which causes the Adam-Stokes syndrome. Treatment is directed toward stimulating the vagal fibers, by compression or electrical stimulation, bodily and mental rest, bromides, morphine, and the digitalis bodies. All forms may be useless.

A Modification of Typhoid Vaccine.—K. KISSKALT (*Deutsch. med. Wchnschr.*, 1915, xli, 393) points out the fact that the lower the temperature at which typhoid bacilli are killed, the greater is their antigenic power. In preparing typhoid vaccine, the bacilli after being killed are usually preserved in 0.5 per cent. carbolic acid solution. It occurred to the author to omit the application of heat altogether and to kill the bacilli by the addition of 0.5 per cent. carbolic acid. He found that one strain of typhoid bacilli was killed within twenty-four hours by the acid; six strains were killed in forty-eight hours; three strains in thirty-six hours. A suspension of cholera bacilli was destroyed in twenty-four hours. By placing the suspension of bacilli in the incubator at 37° C., death of the bacilli occurred within one day. Under these conditions, 0.25 per cent. carbolic acid kills the cultures relatively quickly. Since some cocci are not killed, and may even grow in 0.5 per cent. carbolic acid, careful technic is absolutely essential. Subcultures, of course, are made to determine that no organisms are living before employing the vaccine. By means of vaccine procured in this way, the author believes it may be possible to secure efficient results with smaller doses of vaccine. He purposes to investigate this question as soon as material is available.

On the Treatment of Leishmaniosis.—G. DI CRISTINA and G. CARONIA (*Deutsch. med. Wchnschr.*, 1915, xli, 396) say that the mortality of infantile leishmaniosis is very high, recoveries amounting to only seven to fourteen per cent., and these are apparently spontaneous and not dependent upon treatment. The authors, therefore, decided to try tartartus stibiatus intravenously, which Vianna had found so useful in the tropical venereal ulcer and the skin ulcer of Brazil, each due to Leishmania. Their method of treatment is as follows: Every second day an intravenous injection of a 1 per cent. aqueous solution of tartartus stibiatus is given, the minimum dose being 2 cg. increasing to a maximum dose of 10 cg. The authors have treated ten cases. Two of these were in the last stages of the disease and died. Of the remaining 8 cases, 5 are cured, 2 are improving under treatment, and 1 died of an acute nephritis which developed after an initial improvement in the patient's condition. It was impossible to determine whether the nephritis was the result of antimony poisoning. The total dosage given the cured cases varied between 25 and 84 cg. The general condition of the patient improves quite rapidly after beginning the treatment, and there is also early improvement in the condition of the blood. The number of parasites found in the spleen steadily diminishes, and, finally, they disappear entirely.

SURGERY

UNDER THE CHARGE OF
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Empyema of the Thorax.—WILENSKY (*Surg., Gynec., and Obst.*, 1915, xx, 50) presents a critical study of 299 cases of acute empyema of the thorax treated at the Mount Sinai Hospital, New York, in the last ten years. More than one-third of the cases occurred in the first two years of life. In the first year, 48 per cent. of the cases were lost; in the second year 31 per cent.; and in the third year 41 per cent. For the rest the average mortality was about 18 per cent. The youngest patient was five weeks old and the oldest sixty-four years, and both recovered. Sixty-six per cent. of the cases followed lobar or bronchopneumonia. In 33 per cent. the empyema occurred as a primary disease. In 2 to 3 per cent. of all the cases, the empyema appeared as a secondary focus to some inflammatory lesion in a distant part of the body. It occurred in the bacteremias, usually of the staphylococcus or streptococcus groups; also after infections of the pharynx and tonsils; after appendicitis, either with or without abscess formation; or after purulent inflammations of the uterus and adnexa occurring in the puerperium or independent of it; after a hemorrhoid operation; and after an infected vaccination ulcer. About 2 per cent. of the patients had both pleuræ involved and many of these died. Wilensky says that whatever the cause of the empyema, the pleural cavity is entirely involved in the majority of cases. No adhesions may be present and the pus may circulate over all the lung surfaces between visceral and parietal pleura. The cases studied are from the records of the hospital and it is not stated that this view is based upon personal observations or upon other authority. According to this conception the dulness in the usual empyema should move as freely as in ascites, which is not in agreement with common experience; and the simultaneous opening on both sides of a double large empyema should be followed by a rapid total double pneumothorax, which is not in accord with Hellin's extensive statistical study and more recent literature. Aseptic purulent exudates are uncommon. A certain number of cases were caused by anerobic bacteria. Murphy's formalin injection method of treatment was tried in 7 cases. Two of these died and 3 are reported as not improved. The largest number of the cases stayed in the hospital only from three to four weeks. It was not stated, however, that the sinuses were closed when the patients left the hospital.

The average mortality for the series was 28 per cent., varying from 50 per cent. in infants to 18 per cent. in adults. The least unfavorable period is between three and ten years of age. Twenty per cent. of the patients die as the result of the primary illness, or of a recurrence of it, or of some other complication or intercurrent disease. Only 8 per cent. die because of the empyema, and half of these die in the first forty-eight hours. Twenty-three per cent. of the patients that recovered had more or less trouble with the healing of their wounds—1 out of every 4.

The Use of Silver Foil in Surgery.—Lexer (*Zentralbl. f. Chir.*, 1915, xlii, 217) found silver foil very advantageous, especially, in wounds of the face and in skin transplantations. On the first change of the dressings, a week after operation, or when the sutures have been left three weeks or more under a cast, they are dry and show no surrounding inflammation, even in regions rich in perspiration. It was shown by bacteriological examinations that the sutures and surrounding parts remained sterile when covered by the silver foil. Eczema and maceration of the skin did not occur when the wound secretions were abundant and kept the dressings moist after delay in changing them. A striking feature is the fine smooth scar which is dependent upon the absence of infection. If the silver foil is washed away with benzin and the scar examined by a magnifying glass, three or four days afterward, the new epidermis is seen covering this scar smoothly from one edge of the wound to the other. This gives the sutured wound a better hold so that one may use very fine sutures. This is of special advantage in plastic operations on the face. The sutures may be removed after five days and the wound covered by more silver foil as long as a dressing seems necessary. Because of this rapid covering of the wound by the skin, Lexer employed the silver foil in skin transplantations and thinks there is no better method. Here, also, he employs only one layer of the silver, instead of four layers as by Halstead who introduced this method in 1894, and covers the silver with smooth sterile gauze. On the removal of the dressing at the end of a week the grafts are found healed. In some spots the epidermis is raised by blood or pus, as when granulations have been removed, but these spots are quickly covered by epidermis after the lifted parts are removed and the underlying granulations have been covered by silver foil. Lexer applied the method to granulating wounds and found that good smooth granulations developed and excess was prevented by the silver. Unhealthy granulations with much secretions were cleansed rather rapidly by the silver.

Treatment of Gunshot Wounds of the Abdomen by Compressing Bandages.—Kelling (*Zentralbl. f. Chir.*, 1915, xlii, 241) after calling attention to the high mortality of these cases and the associated conditions affecting the mortality, says that the first efforts of the surgeon should be directed toward localizing as much as possible the results of the injury to the gastro-intestinal tract. The patients should lie quiet and should be carried to the place for treatment. Scheibe reported that those who lay two or three days on the battle field, showed favorable results. Those wounded below the umbilicus should have the upper part of the trunk raised, while those wounded in the epigastrium should have the pelvis raised. Those with gunshot wounds in the right or left flank should lie on the side injured, because gravity is of the first importance in localizing the escaped gastro-intestinal contents. Kelling urges the use of a compressing bandage of the abdomen. It will be most effective in those cases in which the wound is about in the middle of the abdomen. It will be somewhat less effective in wounds of the epigastric or hypochondriac regions because it can only indirectly compress the space under the ribs above, by contracting the volume of the abdominal cavity. The pressure does not operate to force out the intestinal contents into the surrounding peritoneal cavity, but does quite the reverse. It allows no space into which escaping contents can find its way. Hemorrhage from wounded parenchymatous organs is affected in a similar manner. It is especially important, during transportation, to prevent or diminish changes in the position of the viscera which favor greater escape of intestinal contents, by the use of the compressing bandage. The method of treatment was tested, experimentally, in six large rabbits. The same wound was made on each of two rabbits, the compression bandage being employed in one and not in the other. In one of the first two rabbits, through a small epigastric incision, a 1.5 cm. opening in the anterior wall of the stomach was made. Fluid contents were allowed to escape, when the stomach was replaced, the wound in the abdominal wall closed and the compression bandage applied. The rabbit was killed by chloroform two days later and the section showed the whole abdominal cavity free of peritonitis. The incision ring in the stomach was adherent to the liver and omentum. The second animal, on which exactly the same operation was done, was killed after sixteen hours. General peritonitis with the intestines diffusely red and much fluid in the peritoneal cavity were found. The incision wound in the stomach was in no way adherent. The results in the other four rabbits were very similar. The employment of the compression bandage is most effective when applied immediately after the wound is received.

Ileus Duplex.—Handley (*Lancet*, May 1, 1915, p. 900) presents a study of his observations of the pathology of this condition in the living. Ileus duplex is a condition in which, as the result of a pelvic peritonitis, there is obstruction of the intestine at two points: (*a*) in the ileum, at a point about 3 feet above the ileocecal valve, and (*b*) in the sigmoid colon at the junction of its iliac and pelvic portions. These are the points at which the ileum and colon respectively cross the brim of the true pelvis to enter the pelvic cavity. The segments of intestine paralyzed are two in number: (1) the portion of ileum contained in the pelvis, that is to say, about the lower 3 feet, excluding the last 2 inches; and (2) the portion of the large bowel contained in the true pelvis, *i. e.*, the lowest portion of the pelvic colon and the upper portion of the rectum. Three main reasons are given for its importance: (1) because the condition, though curable by appropriate treatment in the early stage, often passes unrecognized under the pseudonym of general peritonitis; (2) because the duplex nature of the obstruction has not hitherto been appreciated; and (3) because, as might be expected, defects in the pathological conception of the condition have been reflected in imperfect treatment. And in this condition delayed or defective treatment means certain death. Handley has met with the condition fourteen times in some hundreds of abdominal cases of all kinds. The results show that forms of treatment which take into account only the small intestine element in the obstruction give a high mortality. Four out of six cases of simple ileocecostomy died. The two patients who recovered indicate that the large intestine obstruction besides being later in onset, may not always become complete. On the other hand he has no death to record among the three patients treated by ileocolostomy combined with cecostomy. This is the ideal treatment. It appears to matter little whether the anastomosis is made between the ileum and cecum or the ileum and sigmoid, provided in either case that a safety valve to the exterior is supplied by tying a catheter in the large intestine. The anastomosis with the cecum is safer because further removed from the inflamed area. Handley is prepared to admit that a cecostomy is superfluous in a minority of cases but it cannot be safe to do without it. He concludes that peritonitis of the serous surface of the intestine, when it reaches a certain degree, is accompanied by complete paralysis of the involved segment of the intestine. General peritonitis means general paralysis of the intestine, and is accordingly not amenable to surgical treatment. But if the peritonitis is partial, though unlimited by any adhesion barrier, certain segments only of the intestine are paralyzed. If the paralyzed segments can be thrown out of circuit by surgical measures recovery is in such cases possible and even likely.

The Covering of Large Defects in the Skull by Means of Celluloid Plates.—Funke (*Zentralbl. f. Chir.*, 1915, xlii, 257) says that in all small defects of the skull the autoplastic is to be preferred above all other methods. It has certain disadvantages, however. For large defects it is almost impossible to form a single large bone shell to answer the purpose. Usually, it must be broken into several pieces which even when the dura is intact can give rise to troublesome deformity. Heteroplastic methods are best in such cases. Funke has employed celluloid plates in preference to metal plates, cork, hard rubber or horn plates. With careful asepsis and thorough hemostasis, the celluloid plates heal in without trouble in most cases and may remain many years, seven years (Hinterstoisser), eight years (Fräncke). Funke had one case, however, which showed that the celluloid plate underwent changes and did not maintain a firm position. The patient sustained a comminuted fracture of the parietal bone which required the removal of several fragments. Some weeks later when the patient had recovered sufficiently, Funke closed the defect in the skull with a celluloid plate 12 cm. long and 7 cm. wide. Later still a secondary operation was necessary to cover a portion of the plate exposed in consequence of tension on some of the sutures. Afterward it remained covered and gave no trouble for about ten years, when a small sinus developed apparently without cause, and discharged bloody serum. The sinus failed to close from conservative treatment and four months later a second sinus appeared. A few weeks after this an operation was done to remove the plate, which was found broken in several places. These overlapped each other accounting for a faulty closure of the original defect in the skull. The consistency of the plate was now much changed. The pieces were thinner than the original plate, the smoothness of its surface had disappeared, the pieces were soft, had lost their elasticity, and could be rubbed away between the fingers. After thorough removal of the granulation tissue with a sharp curette, the wound was completely closed by sutures. The celluloid plate was originally 2 mm. thick, and it appears that about a year before the sinus developed, the plate had been fractured. At that time the patient was struck by a foot ball in the region of the plate, after which he experienced an unpleasant sensation until without further cause the sinus appeared. Six weeks after the removal of the celluloid plate, a gold plate, 15 cm. long and 9 cm. wide, was introduced and healed in without trouble. Celluloid offered a most useful material because of its firmness, and the ease with which it could be sterilized and modelled. We should strive to find another as useful material without its disadvantages. Funke thinks it may be found in juvelit produced by Fritz Pollak, of Vienna. It is made from phenol and formaldehyde.

THERAPEUTICS

UNDER THE CHARGE OF

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The Intradural Administration of Mercurialized Serum in the Treatment of Cerebrospinal Syphilis.—Byrnes (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 2182) reports 32 cases of syphilis of the nervous system who have been treated by the intradural administration of mercurialized serum. Of the 32 cases, there were 13 of tabes dorsalis, 2 of taboparesis, 3 of cerebrospinal meningomyelitis, and 14 of general paresis. In general the cases of tabes and meningomyelitis have shown the most marked improvement although, in a few instances, general paresis has been distinctly benefited. The improvement in clinical symptoms has been similar to that observed in the Swift-Ellis method. In most of the cases of locomotor ataxia relief of the pains has been decided, the gait has improved, and gastric symptoms have been distinctly alleviated. The reaction following the administration of mercurialized serum is usually mild according to Byrnes. There is some pain in the legs for six or twelve hours, slight nausea, rarely vomiting, and a moderate rise of temperature. All of these symptoms generally subside within thirty-six hours. Byrnes has not observed the sphincter disturbances sometimes seen after the use of salvarsanized serum nor has there been any evidence of renal disturbance or other untoward symptoms. The technique for the preparation and administration of the serum is similar to that employed in the Swift-Ellis method, except that no drug is administered before withdrawing the blood. Sufficient blood is withdrawn from the patient to yield from 12 to 30 c.c. of serum. After the blood has coagulated the serum is pipetted off and if necessary centrifuged for twenty minutes. If diluted serum is to be used, to 12 c.c. of the clear serum is added 1 c.c. of a solution of mercuric chlorid in freshly distilled water so made that each cubic centimeter contains one-fiftieth grain of mercuric chlorid. A sufficient amount of normal salt solution is added to the serum thus prepared to make a total volume of 30 c.c. If the concentrated serum is to be used the same quantity of mercuric chlorid is added to 30 c.c. of serum but there is no special reason for employing this concentrated preparation. Byrnes does not believe that mercurialized serum alone is the only treatment that is necessary in syphilis of the central nervous system, he is of the opinion that it is equally, if not more, efficacious than salvarsanized serum in the local treatment of these diseases. The immediate reactions following its administration are, in general, not so severe as those after the use of salvarsanized serum, and the cell count in the spinal fluid appears to be more quickly reduced. Since preliminary medication is not required, the blood may be obtained at any time; and because of the greater stability of the mercurialized serum it may be prepared at leisure and kept in sealed flasks until it is convenient to administer it. In certain cases of cerebrospinal syphilis, in which the serum Wassermann is negative but in which there are all the indication for intraspinal treatment, Byrnes thinks it unnecessary to subject the patient to the discomforts of an intravenous administration of salvarsan merely for the purpose of securing a preparation for intradural injection. This objection does not arise in the use of mercurialized serum. It is true that in many cases both the blood and spinal fluid show evidences of infection, and in such instances the intravenous dose of salvarsan cannot justly be withheld so that he has frequently given the combined salvarsanized and mercurialized serum intraspinally. Owing to the greater stability of the mercurialized serum Byrnes hopes that a method may be devised by which a permanent preparation can be dispensed in sealed ampoules and thus simplify the whole technique of intraspinal therapy. While it may be unwise to entertain the idea of using a foreign serum, it is not unlikely that human serum may be obtained in sufficient quantities for this purpose.

The Treatment of Tetanus.—Hochhaus, Kreuter, Rothfuchs, Alexander, Kühn, and Müller (*München. med. Wnschr.*, 1914, lxi, 2253–2260) write concerning their experiences in treating tetanus among the wounded. There is a great difference in opinion regarding the efficacy of various methods of treatment. Some report great benefit from magnesium sulphate while others have had no success at all with this method. Kreuter advocates the intravenous and intraspinal use of large doses of serum. Rothfuchs claims to have seen marked benefit from salvarsan in four cases. Alexander states that 8 of his patients, given 10 grams of chloral in a single dose each day, have all recovered while 2 died who received only 5 grams of chloral. This group of patients also received serum besides the symptomatic chloral treatment. Kühn and Müller advocate the use of luminal instead of chloral and other sedatives to control the convulsions. They speak especially of the sodium salt, which because of its solubility of water can be used by subcutaneous injection. They believe it is superior to chloral in that it is less depressing to the heart. Müller has found hot baths to be serviceable in controlling the spasms. He has also made use of tracheotomy in some cases, and speaks of the great relief that may be obtained by this procedure.

Pneumothorax for Hemoptysis.—VON ADELUNG (*Boston Med. and Surg. Jour.*, 1914, clxxi, 200) says that the value of induced pneumothorax to control bleeding from the lungs is not sufficiently appreciated. The medical treatment involves considerable loss of time and subjects the patient to the unpleasant and often harmful by-effects of the drugs used. This is especially true of opium, the most valuable of the drugs used for hemoptysis. Pneumothorax, on the other hand, acts promptly and obviates the disadvantages of drugs. The change of pressure from negative to positive leads to the cessation of hemorrhage. By introducing a little more gas every few days the positive pressure may be maintained so that hemorrhage cannot recur. And meanwhile, unless otherwise contra-indicated, the patient may be allowed to go about instead of being confined to bed. For the purpose of inflation the author uses a portable apparatus modeled after Murphy's original apparatus. More recently Murphy has suggested a simple procedure for emergency cases which consists in introducing a hypodermic needle into the pleural space and allowing atmospheric air to be sucked in until the patient feels distress. The needle is dulled by rubbing it on a stone; a puncture of the skin is made with any sharp instrument. The boiled hypodermic needle is then inserted into the pleural sac, with its outer end covered by sterile absorbent cotton, which filters the air that passes in.

The Intraspinal Treatment of Syphilis of the Central Nervous System with Salvarsanized Serum of Standard Strength.—OGILVIE (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1936) being convinced of the value of the Swift-Ellis method, from observation of results in some 200 treatments, but believing that as in the employment of all other anti-syphilitic medication, the maximum efficiency would more readily be attained if it was possible to increase or decrease the strength of the curative agent, undertook to prepare, *in vitro*, a serum of known salvarsan content that could be safely administered intraspinally. Ogiloie gives the details of his method of preparing the serum for injection in the article. Essentially the method consists in the addition of a salvarsan solution, prepared as for intravenous injection, to fresh blood serum. To 15 c.c. of the serum the desired amount of salvarsan is added, an important point being that the temperature of the salvarsan solution and the serum should be the same when the two are mixed. The serum is gently agitated to thoroughly mix the two and is placed in a thermostat at 37° C. for forty-five minutes. From this it is placed in a thermostat at 56° C. for thirty minutes and is then ready to be administered intraspinally. This serum should be given as soon as possible after preparation and under no conditions should be used when more than three hours old. For repeated use Ogilvie has found that from 0.25 mg. to 0.5 mg. of salvarsan added to 15 c.c. of serum is the safest and most effectual dose to employ. He reports a series of cases in which a total of 75 treatments were given. In 50 per cent. of the treatments there was no reaction of any kind beyond a slight temporary weakness. The remaining 50 per cent. had more or less severe reactions following the treatment, more marked in tabetics in whom lightning pains had been a prominent symptom. The author reports in detail a few of the cases treated on this plan. From a study of these cases it will be seen that the laboratory evidences of active syphilis, as shown by the Wassermann reaction in the blood, and the cell-count, globulin content and the Wassermann reaction in the spinal fluid, were reduced in every instance to a greater or less degree, and that, in the majority, there was a concomitant clinical improvement. As to the permanency of these changes Ogiloie holds a conservative view, since it is yet far too early to draw any definite conclusions. It seems reasonable to believe, however, that those cases that have responded favorably, both clinically and biologically, can be controlled with proper supervision and sufficient treatment. Ogiloie says that this method of treatment demonstrates the practicability of giving salvarsan in small doses intraspinally without jeopardy to the patient. He emphasizes the importance of keeping the dosage within 1 mg. The relatively small amounts of arsenic found in serum salvarsanized *in vivo* (according to the method of Swift and Ellis) suggests that its spirocheticidal properties are not wholly dependent on the salvarsan content, but probably also on the formation of some substances in the blood-serum, with the nature of which we are as yet unfamiliar. It was, therefore, in an effort to preserve, so far as possible, the principles of the Swift-Ellis method, that the plan of first incubating the serum at body-temperature for forty-five minutes was evolved.

Splenectomy in the Treatment of Pernicious Anemia.—Jagic (*Wien. klin. Wnschr.*, 1914, xxvii, 1356) reports very good results in three cases of pernicious anemia where the spleen was removed for therapeutic effect. The general condition of these patients improved at once. The improvement obtained may be described as a symptomatic one as the blood still shows all of the characteristics of pernicious anemia. However, the patients feel well and strong and have gained respectively 17, 24 and 26 pounds in periods of time varying from seven to eleven months. In one of the cases reported there was a recurrence of symptoms after a period of improvement following the splenectomy. Under arsenic this patient again improved to a greater extent than before the recurrence. The author believes that the spleen has a marked influence on the course of pernicious anemia although abnormalities of the spleen do not have a direct causal relation to the disease.

The Effect of Theobromin Sodium Salicylate in Acute Experimental Nephritis.—Christian (*Arch. Int. Med.*, 1914, xiv, 827) says that so far as renal function may be judged from phenolsulphonephthalein excretion in acute experimental nephritis produced by uranium in the rabbit, there is no evidence that theobromin sodium salicylate exerts any constant beneficial action. In the severer forms there is almost no evidence of beneficial action; in the very mild forms there is occasionally evidence of beneficial action but this is too inconstant to justify the conclusion that theobromin sodium salicylate really improves renal function even in the very mild forms of acute nephritis. The results obtained in the rabbit are in accord with the common clinical teaching that diuretics are not indicated in acute nephritis in man; but they are no proof of the correctness of this teaching, for results obtained in rabbits cannot be directly read in terms of man. However, they would seem to lend some further support to the view based on clinical observation that diuretics are not indicated in acute nephritis.

OBSTETRICS

UNDER THE CHARGE OF

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Inversion of the Uterus.—Maxwell (*Jour. Obst. and Gynec. Brit. Emp.*, January, 1915) reports two cases of inversion of the uterus. The first was a primigravida delivered under chloroform by forceps, who had hemorrhage three days after labor. A mass the size of a fetal head projected through the cervix into the vagina. There was retention of urine but no apparent septic infection. The hemorrhage was checked by rest and repeated douches, and the patient was so much better that she left the hospital. She returned several months later, as hemorrhage at the menstrual period had been so profuse that she had become alarmed. On examination, although the uterus had grown smaller, the fundus projected two and one-half inches into the vagina. The uterus was gradually replaced by applying Aveling's repositor under chloroform, varying the size of the cup applied. In forty-three and one-half hours the uterus was in its normal position. Following this the temperature rose to 103° F., and gradually subsided. The patient's recovery was complete, and no further pregnancy has occurred. The second case was a primigravida delivered three days previously by forceps, with some difficulty in the removal of the placenta. On examination a large fetid mass was found in the vagina and delivered externally. Its lower portion was covered with necrotic tissue, fibrin, and shreds of placenta, and the mass bled freely during examination. The uterus was completely inverted. After cleansing with hot solution the uterus was cautiously replaced by dilating the constricting ring and eventually carrying four fingers through the ring with the fundus. The complete replacing took about forty minutes. At first considerable force was used to dilate the constricting ring from below. There was very little shock. The patient remained in an exhausted condition, with symptoms of sepsis and a severe diarrhea, until the twelfth day, when she developed symptoms of pulmonary embolism in the left side. On the sixteenth day she had a sudden left hemiplegia and died in a few hours. No autopsy could be obtained, but a blood culture on the thirteenth day showed no positive growth. Hedley reports two cases of inversion of the uterus, at St. Thomas' Hospital, treated by abdominal section and posterior incision of the uterus. The first was a multipara, delivered some six months before admission, who had an adherent placenta, which was partially removed by the hand. but the manipulation was suspended because of hemorrhage. The patient was in bed for six weeks after confinement, with a thick, yellow, offensive discharge. After getting up she had hemorrhages, with constant backache and headache. On examination the patient was profoundly anemic, the uterus was completely inverted, and around the attachment of the cervix to the vaginal vault was a collar of firm tissue, about one-half inch in depth, formed by the lips of the cervix. Under anesthesia an attempt was made to replace the uterus by pushing upward with one hand and making counterpressure through the abdominal wall with the other. This failing, the lips of the cervix were grasped by volsellum forceps, and pressure was made on the fundus, but without success. As the patient's condition was not good the abdomen was immediately opened and a further attempt made to reduce the inversion by manipulation. This also failing the constricting ring was divided posteriorly, when an assistant was able readily to reduce the inversion by slight pressure through the vagina. The wound in the uterus was closed with catgut sutures, from above downward, including the vaginal portion of the cervix, and the wound in the vaginal wall was closed in the same way. The hemorrhage stopped when the sutures were applied. As the uterus was flabby and dropped back into the pelvis, ventrofixation was done. The patient had moderate fever after the operation, but gradually made a good recovery. The second case was that of a primigravida, who gave birth to a child spontaneously, and the placenta was delivered a quarter of an hour later by expression. Soon after a tumor was seen in the vagina, severe hemorrhage occurred and the patient became unconscious. The tumor was recognized as the inverted uterus and immediately replaced. The patient was kept in bed for three weeks, but suffered from severe hemorrhage. This persisted after she got up, and there had been one attack of very severe pain in the pelvis three weeks after the birth of the child. On examination the patient was exceedingly anemic and the uterus found to be inverted. Manipulation being unsuccessful, the same operation done in the first patient was performed upon this, including ventrofixation. The patient made a good recovery without complications.

Uterine Fibroids Complicating Pregnancy.—Phillips (*Jour. Obst. and Gyn. Brit. Emp.*, January, 1915) describes six cases of fibroids complicating pregnancy and parturition. The first patient, aged thirty-three years, pregnant a few months for the first time, had a fibroid upon the posterior uterine wall, which was causing great irritation. It was readily removed by section, but the patient would not remain quiet and aborted some two and one-half months after the operation. The next patient, an unmarried woman, had three months of amenorrhea and a tumor extending above the umbilicus. On opening the abdomen the omentum was adherent, and when this was separated pus was discharged freely. The tumor was found to be a fibroid uterus broken down with suppuration. It was completely removed, the abdomen cleansed, and a large rubber tube inserted. The patient did well for two weeks and then had intestinal obstruction, caused by the bowel becoming adherent to the scar. A second operation was performed, after which the patient did well. On opening the tumor a three months' pregnancy was found with suppuration at the attachment of the ovum. The interesting question arises, Had some attempt been made to produce an abortion and the fibroid become infected by that means? The third patient was delivered by forceps and made a good recovery until the twelfth day, when fever developed. Under an anesthetic a round tumor could be found, attached to the anterior uterine wall. The patient declined operation and gradually recovered. Two years later she was delivered of a second child and made a normal recovery. No trace of the tumor could be found by vaginal examination. The fourth patient was a multipara, who had hydramnios, manual removal of the placenta, and postpartum hemorrhage. After she recovered from confinement she had a foul vaginal discharge, with fever and quick pulse. On examination a dark, offensive, globular mass, as large as a man's fist, was found in the uterus. This was removed under anesthesia and proved to be a sloughing fibroid. The patient made a good recovery. In the fifth patient, a multipara, a fibroid tumor was recognized at labor. The patient suffered after her recovery from parturition with frequent hemorrhage. When the uterus was removed it was found to be fibroid with beginning malignant change. The sixth patient at her confinement was found to have a fibroid in the anterior wall of the uterus. Her recovery was apparently normal. After eight days vomiting occurred, with sudden and marked distention of the abdomen. At operation coils of the small intestine were found adherent to the fibroid in the anterior uterine wall, which had undergone degeneration. The bowel was separated and hysterectomy performed. The patient made a good recovery. The writer points out the fact that hysterectomy is not advisable in every case. Patients having fibroids repeatedly bear children successfully. When the diagnosis is made the patient should receive constant attention and be under observation. The patient should be warned that the presence of the fibroid adds considerably to her danger. If symptoms of degeneration in the tumor occur, operation should be done at once, myomectomy being chosen, if possible. If the tumor is where it will render spontaneous labor difficult or dangerous the patient may be given a chance to go to viability or term and have Cesarean delivery, followed by hysterectomy. If the fibroid is causing no symptoms, and not likely to interfere with delivery, the patient may be allowed to come into labor, but she will require assistance in labor and complications may arise in the third stage. In most cases operation should be advised after recovery from parturition.

A Fatal Case of Rupture of the Uterus.—FOTHERGILL (*Jour. Obst. and Gynec. Brit. Emp.*, January, 1915) reports the case of a woman, who had had nine previous confinements, delivered at home by version for transverse position. When removing the placenta a rent was discovered in the right side of the uterine wall. On admission to hospital the patient was in collapse from hemorrhage. There was no urine in the bladder and no rigidity of the abdomen. On section a tear in the peritoneum extending forward to the right of the bladder on the anterior abdominal wall and backward nearly to the right kidney was found.

The bladder was separated from surrounding tissues except at the base. The uterus was still attached on the left side, but the cervix and lower segment on the right were badly torn. So great was the laceration that the cecum and appendix were torn from their attachments, and it was easy to remove the uterus entire. An effort was made to draw together the peritoneum and a gauze drain was placed in position. The patient rallied slowly, urine was secreted and voided naturally, but on the evening of the fourth day there were chills, and death occurred on the sixth day. At autopsy an abscess cavity in the pelvis shut off from drainage was found. There was no general peritonitis. The bladder was uninjured; the right ureter could not be traced. The cecum and appendix were normal. Although it is not definitely stated, it is probable that version was attempted in this case without complete anesthesia, because the parts were greatly dilated and relaxed. Abundant experience shows that severe laceration is inevitable when version is attempted without the relaxation secured by complete anesthesia, hence in cases of transverse position the procedure should be considered an operation of magnitude sufficient to secure a competent anesthetizer.

Scopolamin-Morphin Amnesia.—Polak and Beach (*Am. Jour. Obst.*, May, 1915) publish papers giving their experience with this method. As regards doses, Polak rated the dose by the condition of the patient, using but one dose of morphin hydrochloride. In this way he thinks he avoided cyanosis in the infant. In 155 cases there were three failures, 150 had no recollection of labor after the second injection, a few had intervals of memory; 10 per cent. had delirium during the stage of pressure on the perineum. There was no fetal mortality. The percentage of patients requiring delivery by forceps was low. There was no postpartum hemorrhage and apparently the secretion of milk was not influenced. In expert hands, in maternity hospitals, in selected cases, the method has usefulness in the first stage of labor. Beach gives the results in 876 cases, in 90 per cent. of which there was some relief from labor pain; there was complete absence of memory regarding labor in 75 per cent. It is a mistake to apply the method to patients first seen when late in labor. So great is then the disturbance that the drugs do not act in the manner desired. Beach considers the method one in which to get the best results it must be used in ideal surroundings with minimum possible doses, and by some one who has trained himself to do this work.

Pregnancy Complicated by Myxedema.—Nyulasy (*British Med. Jour.*, June 19, 1915) describes the case of a primipara, eight months, with albuminuria and myxedema. The patient had a deformity of the spine which lessened the capacity of the pelvic brim. She was apathetic, remaining in bed most of the time, and redness appeared on the skin over the lumbar region from pressure. The patient was delivered by section. The child was macerated and breathed for a short time feebly. The patient's ovaries were apparently normal, but the subcutaneous fat was very tough, pale, fibrous and tightly bound down. The patient speedily made a good recovery.

GYNECOLOGY

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Bulgarian Bacillus in the Treatment of Alkaline Cystitis and Pyelitis.—A very favorable report is given by HAGNER (*Surg., Gynec., and Obst.*, 1915, xxi, 95) on a method of treatment originally suggested by Caulk for these very troublesome conditions by means of instillations of a suspension of lactic acid bacilli. Numerous attempts have been made in the past to render the urine acid in cases of severe cystitis associated with alkalinity of the urine, but usually without much success. Chemical substances injected are soon washed out, and attempts to inoculate the Bacillus coli communis have usually resulted in failure, this organism being overgrown by the proteus vulgarus, which is usually present in these cases. The lactic acid bacillus is, however, as is well known, extremely resistant, and is itself able to overgrow and destroy many other types of organisms. It was upon this theory that Caulk originally suggested its use in the treatment of alkaline cystitis. Hagner has tried it in a number of cases of bad cystitis, and in one of a right pyelitis with alkaline urine, and has been exceedingly pleased with his results. The method of application is exceedingly simple. The bladder is first irrigated with sterile water, as any antiseptic solution might interfere with the growth of the bacillus; three or four of the commercial bulgarian bacillus tablets are then dissolved in an ounce of sterile water, well stirred, and injected into the bladder, the patient being told to retain the fluid as long as possible. This process repeated for three days will usually, the author says, transform an offensive alkaline urine into an acid one, with corresponding rapid amelioration of symptoms. In the pyelitis case the infecting organism seemed to be the Staphylococcus aureus, purulent alkaline urine, containing this in pure culture being obtained from the right kidney, while that from the left was but faintly alkaline, and contained but a small amount of pus. The right kidney pelvis was injected with 7 c.c. of 4 per cent. silver nitrate solution, but two days later the urine still contained pus and was alkaline. Two bulgaricus tablets were then dissolved in 10 c.c. of sterile water and injected through the ureteral catheter. At the end of thirty-six hours the patient had a chill, and rise of temperature to 103.5° but dropping to normal in twelve hours. The following day the urine was acid; two further injections were given into the bladder, but not into the kidney; after three months the urine remains clear, acid, and free from pus.

Thorium, a New Agent for Pyelography.—A few months ago we spoke of the desirability of obtaining some substance capable of throwing a Roentgen-ray shadow when injected into the kidney pelvis, and yet perfectly harmless under all circumstances to the renal tissue, conditions that are not entirely fulfilled by collargol, and similar preparations which are chiefly used for this purpose at present. From the Urologic Department of Johns Hopkins there has recently come a report by Burns (*Jour. Am. Med. Assn.*, 1915, lxiv, 2126) on the use of thorium for pyelographic work. Thus getting away entirely from the silver preparations, some form or another of which have been used by most previous workers. Thorium nitrate, the author says, dissolves readily in water, giving a clear markedly acid solution, which is opaque to the Roentgen rays, but is too irritant for use in the bladder. The neutral solution of thorium nitrate and sodium citrate, however, seems to possess the important characteristics of being non-toxic, non-irritant, and fluid, so as immediately to escape from the ureters and bladder, while at the same time casting a clear, distinct Roentgen shadow. It is perfectly clear to transmitted light, possessing in large volume a faint yellowish tinge. It is much cheaper than the silver preparations, an advantage when it must be used in large quantities for bladder pictures or large hydronephroses. The solution now being used is made as follows: "Ten grams of thorium nitrate are dissolved in as little distilled water as possible, to this solution, kept hot on a water or steam bath, are added 30 c.c. of a 50 per cent. solution of sodium citrate, the additions being made in small quantities, and care being taken to shake the solution thoroughly after each addition. At first after the addition of the citrate solution, a white gummy precipitate is formed which later becomes granular, and finally dissolves on the addition of all the citrate solution. This solution is then made neutral to litmus by the careful addition of a normal solution of sodium hydroxide, and made up to 100 c.c. with distilled water. On filtration, a clear, limpid solution is obtained, which, when sterilized, either by boiling or steam under pressure, is ready for use. The stability of the solution is not affected in the least by sterilization." Burns states that this solution is now being used in all their suitable urologic cases, and appears to be perfectly innocuous. It gives excellent shadows, as the photographs accompanying the article testify.

Urinary Incontinence in the Female due to Diverticulum of the Urethra.—An exceedingly interesting case of this rather unusual condition has recently been reported by Jarecki (*Ztschr. f. urol. Chir.*, 1915, iii, 241). The patient was a girl, aged twenty-one years, a nullipara, who had complained of incontinence since early childhood. The incontinence was not complete, but occurred on laughing, coughing, or making sudden movements of any kind, particularly if the bladder was at all full. Even at night, however, during deep sleep involuntary micturition often occurred. The act of voiding was never accompanied by burning or pain. Cystoscopic examination revealed what appeared at first to be a perfectly normal bladder, with a good sphincteric ring. Just as the examiner was about to conclude that the findings from this stand-point were entirely negative, however, the sphincter was seen in the cystoscope to dilate appreciably, so that the instrument could be drawn out into a distinct saccular dilatation of the proximal urethra, or "Vorblase," as the author calls it. This was at least the caliber of the thumb, lined with smooth mucosa, but with a somewhat trabeculated wall. It was possible to examine this sacculation only for a moment, the walls almost immediately falling together again. It was found, however, that if the patient was told to make an effort to void urine with the cystoscope in place, the sacculation immediately reappeared, the sphincter opening wide, and the sac again filling with urine. From these findings the conclusion was reached that the incontinence probably had two factors in its causation: (1) a weakness of the vesical sphincter, this being especially important when the bladder was overfilled, and (2) an emptying outward of the urethral diverticulum, this occurring usually shortly after completed micturition. It appeared evident, therefore, that in order to cure the condition bóth these factors must be dealt with. Attempts were made to effect a cure by various procedures, four separate operations being required before a satisfactory result was obtained. All efforts to simply plicate or infold the dilated portion of the urethra, without opening and resecting a portion of it, proved failures, and eventually it became necessary to make a longitudinal incision through the anterior vaginal wall and through the wall of the sacculated urethra, excising a portion of the latter, and closing the opening with sutures passed not quite through the mucosa. A piece of fascia lata 4 mm. broad was then excised, and wrapped completely around the proximal portion of the urethra, the ends being united with catgut sutures. At a previous operation a circular suture of silk had been passed about the neck of the bladder through a supra-pubic incision, in the attempt to strengthen the action of the sphincter. The final result is reported by the author as entirely satisfactory, the patient having regained complete control of her urine, a condition which has lasted two years since operation. Jarecki thinks the origin of the trouble was probably a primary weakness of the vesical sphincter, which permitted a filling of the proximal portion of the urethra whenever the bladder became distended, involuntary passage of this urine being prevented at first, however, by the action of the smooth and striped muscle of the urethra. With the gradual dilatation of the posterior portion of the urethra that occurred under these conditions, the sufficiency of these auxiliary muscles became impaired, and thus the condition of partial incontinence developed.

Ovarian Sarcoma in Children.—Three cases of large sarcomatous ovarian tumors occurring in young girls are reported by HIGGINS (*British Jour. Child. Dis.*, 1915, xxi, 161). The first case was in a child, aged five years; a swelling had been noticed in the abdomen for six weeks, and the child was obviously extremely ill on admission to the hospital. Blood was passed in small quantities from the vagina. On opening the abdomen a tumor weighing three and one-half pounds was found springing from the right ovary, the other being apparently normal. The tumor was removed, and proved histologically to be a mixed-cell sarcoma; operation was followed by Roentgen-ray treatment for thirteen weeks, at the end of which time the child appeared entirely strong and healthy. The second case was a child, aged ten years, from whose right broad ligament a hard tumor the size of a cricket ball was removed by operation. In this case a lump in the abdomen had been noticed about five weeks previously. This tumor likewise proved to be a mixed-cell sarcoma; over two years later, however, the child was still in perfect health. The third case was a child, aged seven years, in whom a solid tumor the size of a cocoanut was found at autopsy; this neoplasm grew from the right ovary and weighed five and three-fourths pounds. It had burst through its capsule and invaded the adjacent omentum, intestines, and liver, but there were no glandular enlargements or distant metastases. Microscopically it proved to be a round-cell sarcoma. In this instance the child's illness had been of four or five months' duration, and no attempt had been made to remove the tumor by operation. The author calls attention to the fact that in all these cases there was an insidious onset of symptoms, with unexplained colicky pain, and later the appearance of a mobile lump in the abdomen, with steady enlargement of the latter, and pain and fever, the result of adhesive peritonitis. He considers these tumors entirely analogous in genesis to the much more common malignant kidney growths, and avises immediate operation in every instance as soon as even a provisional diagnosis is arrived at.

OTOLOGY

UNDER THE CHARGE OF

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Physiology of the Labyrinth Windows.—In accordance with the observations of Kessel, Panse, and Bárány and others, MAURICE (*Arch. internat. de laryng.*, 1914, xxxvii, 2) refers the improvement in hearing consequent upon the application of a cotton artificial drumhead, over the round window, to the physiological functions of the two labyrinth windows, the one supplementing the other by the reverse movement of its membranous structure in response to the impact of a sound wave. When a sound falling upon the membrana vibrans, and transmitted through the ossicular chain, reaches the membrane of the oval window and meets the resistance of the incompressible intralabyrinthine fluid it can proceed no further except that the membrane of the round window, moving consonantly outward, permits transmission of the movement actuating the membrane of the oval window, through the mass movement of the otherwise acoustically immobile fluid. If the sound wave passing through a perforation in the membrana vibrans falls equally, and coincidently, upon the membranes of the two labyrinthine windows there will be no resultant sound perception because of the lack of provision for mass movement in response to an unilateral impact; if, however, the sound wave impact is shut off from one or the other window the primary and secondary movements of the window membranes are facilitated and, with the consequent molar movement of the intralabyrinthine fluid, the cochlear end apparatus is actuated and the sound perceived. In the practical application of the cotton artificial drumhead soaked in melted vaseline, or albolene, a minimum pressure should be exerted upon the membrane of the round window as compared with that brought to bear upon the stapes or the membrane of the oval window; care should also be taken to leave no enclosed air space between the membrane of the window and the cotton tampon, the space in question acting as a resonance chamber and serving therefore to reinforce certain tones and give the effect of autophany. The peculiar variations in hearing incident to suppurative processes in the middle ear, with perforation of the drumhead, and especially the better hearing when the middle ear is moderately moist with discharge, is accounted for by the fact that the presence of the fluid, in the more dependent portion of the cavity, somewhat inhibits the movement of the membrane of the round window and leaves it free to respond, correlatively, to the impulse received at the oval window and transmitted through the medium of the intralabyrinthine fluid.

Aural Sounds of Muscular Origin.—The observations of DEDEK (*Monatschr. f. Ohrenh.*, 1914, xlviii, 3) upon both subjective and objective noises in the ear, of muscular origin, include not only the intrinsic muscles of the sound transmitting apparatus of the middle ear, but also those having their origin in the movement of the palatal and tubal muscles especially, but occasionally resulting from the action of such extraneous muscular bundles as the attolens and attrahens auriculæ. One illustrative case had its origin in spasmodic contraction of the pharyngeal muscles developing as the result of a traumatic neurosis and comparable to the sound of the ticking of a watch or the snapping of the finger nails, recurring as often as one hundred and forty times in a minute, multisynchronous neither with the patients pulse nor breathing, and audible, in stillness, at a distance of five meters. There was no determinable movement of the membrana tympani but distinctly visible movement of the soft palate accompanied by similar movements of the neck and, sometimes, of the face muscles, all of these movements being synchronous with the objective sound. Checking of the palatal movement, holding the breath, depression of the tongue or tickling of the nasal mucous membrane caused a cessation of the muscular activity and consequently of the produced sound but catheterizing or even bougieing of the tympanopharyngeal tube had no similar effect. Inspection of the faucial opening of the tube during the production of the sound showed a very slight vertical movement of the wide open tube. The psychic condition of the patient had an evident influence upon the intensity of the sound produced and the muscles principally implicated were the tensor and levator veli in addition to the salpingopharyngeous.

Subsequent Dressings of Mastoid Operations.—WEISSMANN (*Rev. hebd. de laryng.*, 1914, No. 19) practices, and advises, as the best method of after-treatment of mastoidectomies, whether acute or chronic, whether the antrum be opened or the mastoid cavity completely evacuated with inclusion of the bony wall of the middle and posterior fossæ, primary closure of the postaural wound without drainage. The exceptional cases are those in which an intracranial complication has to be considered, an extradural abscess or possibly a wound of the sinus; these cases are, primarily, to be packed, but the tampons omitted so soon as there is no longer danger of hemorrhage or other complication. The stitch closure of the postaural wound is also contra-indicated in cases of coincident subcutaneous abscesses, infiltration and maceration of the dermis and in the presence of fistulous openings; even under these conditions the author dispenses with packing and applies only a superficial dressing and bandage. In the cases of primary closure if, at the end of eight days, the ear is not becoming dry and the postaural wound is not in good condition the stitches should be removed and the wound opened and drained. The author further advises the primary and complete closure of the postaural wound in the radical operation, as well as in the simple mastoid exenteration and also the omission of gauze wicks in the external auditory canal. On the fifth or sixth day the bandage and dressings are removed and, if there is much discharge or offensive odor, the wound is syringed with boiled water to which a moderate amount of hydrogen dioxide is added; on the eighth day the stitches are removed and on the tenth day the postaural bandage is dispensed with and the subsequent treatment is that customarily applied to an uncomplicated suppurative process in the middle ear with frequent mild antiseptic cleansing followed by insufflation of boric acid powder and similar substances. All of the cases of this class should be continued under careful and stated observation in order to attain the best results. The contra-indications to a primary stitch closure of the postaural wound in the cases of radical operation and the precendent application of gauze packing are the same as in cases of the simple mastoid operation.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Butyric Acid Sclerosis of the Arteries. Metchinkoff claimed that the products of bacterial fermentation in the bowel were important factors in causing a chronic intoxication and arteriosclerosis. He was able to demonstrate the effect of paracresol in this manner. The importance of this intoxication, he believes, does not lie in heavy individual doses, but rather in the cumulative effect of the absorbtion of small quantities. In a similar manner Dratchinski was able to experimentally reproduce arterial lesions by feeding small quantities of indol over a long period of time. Following a suggestion by Metchinkoff, Coleman (*Ann. de l'Inst. Pasteur,* 1915, xxix, 139) studied the effect of butyric acid absorbed from the bowel upon the arterial system. He points out that different quantities of butryic acid are found in the intestinal contents, the quantity in some individuals being much higher than in others on account of bacterial decomposition. Certain anerobic bacteria (B. Butyricus, B. Welchii, B. sporogenes) are particularly prone to produce butyric acid in the intestine. A fair amount of this acid is absorbed and appears in the blood. Nine guinea-pigs were carefully studied and four of them were found with "cartilaginous" plaques in the aorta. Calcareous masses were not present in any of the arteries or organs. His figures agreed with those of Dratchinski who found that 50 per cent. of the guinea-pigs had "cartilaginous" plaques in the arteries. Coleman then attempted to feed guinea-pigs with butyric acid and found that it had to be greatly diluted to prevent gastric disturbances. The calcium butyrate is still more poisonous than the acid itself. 0.5 c.c. of a 12.5 per cent. solution of caclium butyrate were given by the mouth. In another series small doses of butyric acid were given. The experiments were continued from twelve to twenty-nine weeks. Calcification of the aorta was commonly found in these cases associated with calcareous deposit in the kidneys. Sclerosis was also present in the arteries of different organs. The changes in the aorta were accompanied by a fatty degeneration of the muscle cells, as well as a sclerosis of the vasa vasorum. He believes that these organic changes are the direct result of the butyric acid or its salts.

Syphilitic Leptomeningitis.—Very little attention has been given to the syphilitic lesions of the meninges unless gummata were present. Types of pachymeningitis of syphilitic origin were also recognized, but it was not until in 1908, when Duerck reported five cases of acute syphilitic leptomeningitis, that attention was attracted to this subject and active discussion begun. On the whole, the type described by Duerck was rather unusual. LeCount and Dewey (*Jour. Infect. Dis.,* 1915, xvi, 142) studied the leptomeninges in a series of autopsies with the view of noting the presence of meningeal change in undoubted cases of syphilis as well as for the recognition of lesions of the meninges in conditions other than syphilis. They recognized three main types of changes in the pia: (1) opacity, (2) patches of fibrous thickening, (3) discreet focal lesions. Opacity of the pia is commonly present in a great variety of diseases. Its distribution is variable as is also the amount of opacity. Patches of fibrous tissue in the pia are not uncommonly associated with opacity and the two appear related. The focal lesions are more commonly seen at the base on the under surface of the frontal and temporal lobes and the pons and cerebellum. Vascular changes at the base were not infrequent, while pial hemorrhages were found in several cases. The nodular type of meningeal change is the one deserving particular attention, in connection with syphilitic meningitis. In all, the authors have described fifty-five cases. They concluded that the finding of meningeal lesions of a focal character necessitates the exclusion of syphilis as a cause before suggesting other infections as the etiologic factor. Such nodular lesions of the meninges should be given a value equal to lesions in other places as the aorta or liver for the final summing up of evidence for syphilitic infections. The arachnoid scars show that this membrane is one of the few places where organisms find conditions favorable for a limited multiplication after generalized spirochetemia. They point out that the evidence that alcohol may produce a fibrous meningitis is inadequate.

The Mechanism of Phagocytosis.—Much has been taken for granted in our conception of the manner in which animal cells ingest solid particles and the work of recent years has concerned itself with the more intricate points of bacterial destruction within the bodies of leukocytes. KITE and WHERRY (*Jour. Infect. Dis.*, 1915, xvi, 109) suggest that foreign particles are taken up by leukocytes because the latter have sticky surfaces. These particles adhere to the cell and are carried into the interior by cytoplasmic streaming currents. This mode of dealing with foreign particles can be observed in the amebæ of the limax group, which, while in the trophozoit stage, are provided with sticky surfaces. These amebæ while in the motile flagellate stage are not sticky. The effect of opsonins upon bacteria is to cause their outer surface to become sticky. The authors repeated a number of tests with opsonins and found that when separately incubated mixtures of leukocytes and serum and serum and bacteria are agitated together, many of the bacteria stick to the leukocytes and are rolled into their substance. Such bacteria undergo digestion. Experiments with a minimum amount of agitation show that phagocytosis is reduced. They believe that bodies similar to bacteria stick to leukocytes best in the presence of unheated serum because they absorb something from the serum which makes them more sticky and hence their chances of adhering to the surfaces of the leukocytes are increased.

Multiplicity of Tumors.—EGLI (*Cor.-Bl. f. schweiz. Aertze,* 1914, 449) studied the autopsy material of the Pathological Institute of Basle. In 4765 post mortem examinations, 966 tumors were found and of these 263 (27.2 per cent.) showed the presence of multiple tumors. The author classifies the various combinations of multiple tumors. He believes that the presence of multiple tumors is accidental and that there is no influence exerted by one type to induce the appearance of another. There was also lack of evidence of a predisposition for either benign or malignant tumors. The nature of a tumor is dependent upon the character of the cell component as well as the influence of the surrounding tissues. These two factors appear to guide the growth of tumor masses toward the benign or malignant types.

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ORIGINAL ARTICLES

OUR EXPERIENCES WITH GASTROENTEROSTOMY: A STUDY OF ONE HUNDRED CASES AS COMPARED WITH A SIMILAR NUMBER OF CASES OF PYLOROPLASTY.[1]

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A year ago we reported our thirteen years' experience with pyloroplasty, and from a study of 100 cases the following conclusions were drawn:

1. The operation has certain advantages over gastroenterostomy, and but few of its disadvantages.

2. The operation has its greatest indication in the relief of pyloric stenosis due to chronic ulcers, situated at or near the pylorus, and on either side of it, or resulting from cicatricial contraction following the healing of such ulcers. It is often a useful procedure in cases of hemorrhage due to gastric ulcers on the lesser curvature, or to duodenal ulcers which cannot be controlled medically, and which threaten the life of the patient, as well as in the chronic dyspepsias due to ulcers which have not been relieved by medical treatment.

3. The special advantages of this operative procedure lie in its affording the opportunity to excise all ulcers whether perforated or

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[1] Read at the Meeting of the American Gastroenterological Association, in Baltimore, Maryland, May 11, 1915.

not in the anterior walls of the stomach or duodenum after direct inspection of the part affected; also the application of treatment to ulcers situated in the posterior walls. It does not greatly disturb the normal relation between the stomach and intestines, as is the case in other operations.

4. Such objections as are urged against the operation, *e. g.*, its inapplicability in the presence of adhesions surrounding the pylorus, as well as in the presence of active and bleeding ulcers, and also because of the fact that the new opening is not at its lowest point, taking advantage of gravity, are according to our experience more fanciful than real, since the operation has frequently been performed under these conditions with most gratifying results. The interesting experimental work of Cannon and Blake and others supports this contention.

5. The only contra-indications to the operation are inability to mobilize the duodenum when adhesions are too dense, and thickening and infiltration about the pylorus due to hypertrophic forms of ulceration. These conditions, however, in our experience occur but rarely.

6. In atony or gastroptosis with slight motor insufficiency such as is observed in the water-trap stomach, or in nervous dyspepsia, *i. e.*, in gastric disturbances not dependent upon organic disease, this operation is contra-indicated.

7. From our experience with the operation the immediate as well as the final results are most encouraging. While in some instances partial gastrectomy or gastroenterostomy is undoubtedly the operation of choice, nevertheless, on account of its simplicity and because of its satisfactory end results, we believe that pyloroplasty will continue to retain its position as a safe and useful procedure.

Inasmuch as our results with pyloroplasty appeared to be so much more satisfactory than with gastroenterostomy, it seemed to us that it would be well to bring together the results of the later operation, compare them in detail with those of pyloroplasty, and determine whether any advantage really existed in favor of pyloroplasty. For this reason we have collected together 100 cases taken consecutively, beginning in 1902 the date at which the operation of pyloroplasty was first introduced. In gathering our experiences we deem it most important, as with our pyloroplasty cases, that not only should the immediate effects be noted, but also the final results, that is, the results obtained after a term of years.

It is also of importance to note that only those cases have been included in this report in which the gastroenterostomy was performed for other than malignant conditions. All cases in which there has been the slightest question of malignancy have been excluded from this series.

Of the gastroenterostomy cases the immediate results were noted in all cases; the remote results in 74 cases.

In analyzing our results we note that the largest proportion of cases in which it was performed occurred between the thirtieth and sixtieth years.

CASES ARRANGED ACCORDING TO AGE.

Years.	No.	Per cent.	Years.	No.	Per cent.
20 to 25	6	6	45 to 50	12	12
25 to 30	7	7	50 to 55	15	15
30 to 35	10	10	55 to 60	12	12
35 to 40	14	14	60 to 65	5	5
40 to 45	16	16	65 to 70	3	3

Of the total number there are 56 males and 44 females. The following tables illustrate the number of cases observed in males and females according to age:

	Males.		Females.		Total.	
Years.	No.	Per cent.	No.	Per cent.	No.	Per cent.
20 to 25	2	2	4	4	6	6
25 to 30	4	4	3	3	7	7
30 to 35	6	6	4	4	10	10
35 to 40	6	6	8	8	14	14
40 to 45	10	10	6	6	16	16
45 to 50	8	8	4	4	12	12
50 to 55	8	8	7	7	15	15
55 to 60	6	6	6	6	12	12
60 to 65	4	4	1	1	5	5
65 to 70	2	2	1	1	3	3
Total	56	56	44	47	100	100

The duration of the symptoms in our cases varied greatly, ranging from one month to nineteen years, the average duration being nine and a half years.

The following table presents the cases grouped according to the duration of symptoms:

CASES GROUPED ACCORDING TO DURATION OF SYMPTOMS.

Time.	No. of cases.	Time.	No. of cases.
1 month	1	7 years	8
2 “	2	8 “	6
3 “	1	9 “	2
4 “	1	10 “	2
6 “	4	11 “	3
7 “	2	12 “	1
9 “	1	13 “	1
11 “	3	14 “	2
1 year	10	15 “	3
2 years	8	16 “	2
3 “	14	18 “	2
4 “	7	19 “	2
5 “	12		

Average duration of symptoms, nine and a half years.

We have noted the principal symptoms observed in both males and females at various ages. Of these pain was observed in 90 per cent.

of cases (51 males and 39 females); vomiting occurred in 65 per cent. of cases (36 males and 29 females); hematemesis in 23 per cent. (18 males and 5 females); melena in 44 per cent. (28 males and 16 females); retention in 36 per cent. (19 males and 17 females).

PRINCIPAL SYMPTOMS OBSERVED.

	Pain.			Vomiting.			Hematemesis.			Melena.			Retention.		
Age.	M.	F.	Total.	M.	F.	Total.	M.	F.	Total.	M.	F.	Total.	M.	F.	Total.
20 to 30 years .	4	6	10	4	5	9	1	0	1	3	6	9	2	2	4
30 to 40 " .	11	10	21	8	6	14	4	2	6	7	5	12	6	6	12
40 to 50 " .	17	10	27	12	8	20	8	2	10	9	2	11	7	6	13
50 to 60 " .	13	12	25	8	9	17	4	1	5	6	3	9	2	3	5
60 to 70 " .	6	1	7	4	1	5	1	0	1	3	0	3	2	0	2
Total . .	51	39	90	36	29	65	18	5	23	28	10	44	19	17	36

In the following table we have arranged the cases of gastric and duodenal ulcers according to age and sex. There are 46 cases of gastric ulcer (32 males and 14 females) and 38 duodenal ulcers (15 males and 23 females) making a total of 84 cases. In addition gastroenterostomy was performed upon 4 cases for gastroptosis, in 2 for pylorospasm, and 9 for pyloric stenosis, due to adhesions (2 due to cholelithiasis, 7 due to adhesions of undetermined cause, probably old healed ulcers). One case presented both gastric and duodenal ulcers.

GROUPING OF THE GASTRIC AND DUODENAL ULCERS ACCORDING TO AGE AND SEX.

	Males.		Females.	
Age.	Gastric. No.	Duodenal. No.	Gastric. No.	Duodenal. No.
20 to 30	4	1	2	3
30 to 40	6	2	2	8
40 to 50	12	5	3	6
50 to 60	8	4	6	6
60 to 70	2	3	1	0
Total	32	15	14	23

Of the 84 cases, obstruction of the pylorus occurred in 67 instances. The obstruction was due in 44 cases to gastric ulcer, in 14 to duodenal ulcer, and in 9 to adhesions. There were 4 cases in which gastroenterostomy was required as secondary to pyloroplasty.

CASES REQUIRING GASTROENTEROSTOMY AS SECONDARY TO PYLOROPLASTY.

Age.	Sex.	Cases.
58 years	F.	Pyloric obstruction due to adhesions produced by gall-bladder infection eleven years after pyloroplasty.
52 "	M.	Duodenal ulcer formed five years after pyloroplasty.
48 "	M.	Infected sutures causing immediate obstruction at site of pyloroplasty requiring gastroenterostomy after five days.
11 "	M.	Duodenal ulcer after one and one-half years.

In one case there occurred a pyloric obstruction due to adhesions produced by cholecystitis eleven years after the pyloroplasty. In the second, a duodenal ulcer formed four years after the pyloroplasty. In the third infected sutures (linen thread) caused early obstruction at the site of the pyloroplasty, and in the fourth, a duodenal ulcer formed after a year and a half. In all of these cases secondary gastroenterostomies had to be performed, which gave entire relief. In our gastroenterostomy cases secondary operations were necessitated in four instances. In one case there was a vicious circle; an entero-anastomosis was made on the day following the operation, and the patient died two days later. In two instances the gastroenterostomy opening became obstructed by adhesions, after one year and one year and a half respectively, secondary gastroenterostomies were performed.

In a fourth instance a secondary gastroenterostomy was performed after the old gastroenterostomy opening had become obstructed after a period of three years.

CASES REQUIRING SECONDARY GASTROENTEROSTOMIES.

Cases.	Age.	Sex.	Cause.
I . .	70 years	M.	Vicious circle.
II .	24 "	F.	Obstruction from adhesions after one year.
III .	35 "	F.	Obstruction from adhesions one and a half years.
IV .	53 "	M.	Obstruction from adhesions after three years.

It is only fair to call attention to the fact that some of the earlier of the gastroenterostomies were performed by the method then in vogue—namely, the anterior long-loop anastomosis, which did not yield so satisfactory results as those obtained by the no-loop posterior anastomosis. By far the larger number, however, were done after the latter method.

The following table illustrates the immediate results of gastroenterostomy of the 100 cases, consisting of 56 males and 44 females; the operations proved satisfactory immediately in 45 males and 37 females (82 per cent.) and unsatisfactory in 11 males and 7 females (18 per cent.).

In contrast with the immediate results of pyloroplasty, postoperative nausea and vomiting are not infrequent after gastroenterostomy. There are but few instances in our series in which marked nausea did not appear; vomiting was present in 72 of our 100 cases, while flatulency and distention were not infrequent. When one notes the great freedom from discomfort following immediately after pyloroplasty, there can be no question as to the distinct immediate advantage of this procedure over gastroenterostomy.

It is but fair to state, however, that the nausea and vomiting have been at times induced by improper feeding, produced by overdistention and weighing down of the fundus, and thus tending to produce a temporary closure of the new opening. In a number of instances this condition was overcome by relieving the overdistention and increasing the tone of the stomach by means of lavage.

Diarrhea after operation appeared in eight instances, mainly, however, after the first week or ten days, and was usually due to errors in diet. Inasmuch as the operation is performed in most instances upon patients affected with pyloric obstruction, and after having had this condition for years, it is easily understood how, on account of the rapid passage of the gastric contents through the stomach, a weakened intestine may be overtaxed and intestinal indigestion and diarrhea be induced. On this account, as well as because the stomach has in most instances temporarily lost its tone; and inasmuch as in some cases active ulcers are still present, we have found it advisable to regulate the diet following immediately upon operation and continuing on for several months according to the following plan, which has been found very satisfactory. On account of the frequent occurrence of gastrointestinal upsets after gastroenterostomy we have, according to our experience, found it more important to follow the following dietetic restrictions than after pyloroplasty.

For two days after operation nourishment is administered only by means of rectal alimentation. Normal salt solution or plain water, after Murphy's method, is begun immediately after operation, with nutrient enemata at intervals of every four hours on the second and third days. On the third day after operation, egg-albumin is given in teaspoonful doses, gradually increased to one-half ounce every two hours on the fourth day and two ounces on the fifth day. On the eighth day any liquid is permissible, and on the eleventh day the patient is given a soft-boiled egg; on the thirteenth, soft diet; on the fifteenth, very restricted light diet; on the sixteenth, a restricted light diet; on the eighteenth day, light solid food. Small quantities of water at a time are allowed by mouth after twenty-four hours.

Diet List following the Operation of Gastroenterostomy. First day, first twelve hours, nothing by mouth; nutrient enemata every four hours alternating with continuous salt solution by Murphy's method.

First day, second twelve hours: water in dram doses.

Second day: increase water gradually up to 1 ounce every two hours.

Third day: water 1 ounce, alternating with albumin, 1 dram.

Gradually increase quantities of each until

Eighth day: any liquid 2 ounces every two hours.

Ninth day: any liquid, 3 ounces every two hours.

Tenth day: any liquid, 4 ounces every two hours (discontinue rectal feeding).

Eleventh day: one soft-boiled egg in addition to any liquid.

Twelfth day: two soft-boiled eggs in addition to any liquid.

Thirteenth day: soft diet.
Fourteenth day: soft diet.
Fifteenth day: very restricted light diet.
Sixteenth day: restricted light diet.
Seventeenth day: restricted light diet.
Eighteenth day: any digestible solid food.

After the eighteenth day the following diet list may be gradually followed, and should be continued for at least four or five months: Soups: any light soup. Meats: any of the easily digestible meats, as brains, sweetbreads, beef, mutton, lamb, or poultry (best minced, and taken either broiled or boiled). Fish: mainly the white variety, mackerel, rock, bass, as well as oysters (boiled or broiled). Eggs: in any form except fried. Vegetables: best taken mashed and strained; the easily digestible forms, as asparagus, spinach, peas, beans, potatoes, carrots. Farinaceous food: any of the cereals; bread to be taken stale. Desserts: any of the light puddings. Fruits: mainly stewed. Fatty food: cream, butter, and olive oil. Drinks: milk, buttermilk, cocoa, carbonated mineral water, and plain water.

The following must be avoided: Rich soups, fried foods, pork, veal, stews, hashes, corned meats, potted meat, twice cooked meat, liver, kidney, duck, goose, sausage, crabs, sardines, lobster, preserved fish, smoked fish, salted fish, salmon, cauliflower, celery, radishes, cabbage, cucumbers, sweet potatoes, tomatoes, beets, corn, salads, bananas, melons, berries, pineapple, hot bread, or cakes, nuts, candies, pies, pastry, preserves, cheese, strong tea, strong coffee, alcoholic stimulants.

IMMEDIATE RESULTS OF OPERATION.

	Males.		Females.	
Age.	Satisfactory.	Unsatisfactory.	Satisfactory.	Unsatisfactory.
20 to 30 years	5	1	5	2
30 to 40 "	8	4	10	2
40 to 50 "	16	2	9	1
50 to 60 "	12	2	11	2
60 to 70 "	4	2	2	0
Total	45	11	37	7

In order to obtain a clear view as to the immediate results of the operation we have compared the gastric secretion in the following two cases of pyloric stenosis due to ulcer, before the operation with that obtained one, two, and three months after operation. The figures given are an average of a number of examinations. The total acidity is first noted, then the amount of free hydrochloric acid, and finally the quantity of contents recovered, which in a measure represents the motor activity of the stomach. It is evident in every case that the total quantity of acid as well as the percentage of free hydrochloric acid, which may be exceedingly high before operation, is gradually reduced to normal, but that this does not occur immediately after operation, but requires about two to three months before the normal is established, after which it continues to remain stationary. Similarly the large quantity of contents obtained is gradually reduced to normal after operation, while the retention observed at first entirely vanishes. It is, therefore, evident that while the secretory and motor functions of the stomach are at once markedly improved after gastroenterostomy, these functions do not usually become normal immediately, but just as in the pyloroplasty cases several months must elapse before perfectly normal conditions are established.

	Total acidity.	Free HCl.	Quantity of contents: After test meal.	On fasting stomach.
M. J. operation: June 27, 1908				
Before operation:				
May 5, 1908	120	74	280	210
After operation:				
July 24, 1908	82	70	100	0
July 30, 1908	62	62	86	0
Aug. 10, 1908	46	38	54	0
Sept. 2, 1908	42	30	50	0
R. R. operation: June 27, 1909				
Before operation:				
May 11, 1909	105	82	310	230
After operation:				
Aug. 2, 1909	100	72	96	0
Aug. 30, 1909	88	66	55	0
Sept. 15, 1909	44	32	45	0

Deaths following Operations. There were seven deaths following immediately upon operation; these occurred from the third to the thirty-third day. In one instance death was due to pneumonia following a secondary gastroenterostomy for a vicious circle; in a second, death was sudden, due to pulmonary embolism; in a third, it was due to toxemia from an intestinal obstruction; in a fourth to persistent vomiting, due to a vicious circle; in a fifth, to exhaustion from a postoperative diarrhea, and in a sixth and seventh to bronchopneumonia in debilitated individuals.

The following table illustrates the number of deaths following immediately upon operation, with cause of death:

IMMEDIATE RESULTS—DEATHS.

No.	Sex.	Day of death after operation.	Cause of death.
I	M.	3	Pneumonia following a secondary gastroenterostomy for a vicious circle.
II	M.	7	Sudden death due to pulmonary embolism.
III	M.	23	Toxemia due to intestinal obstruction from inflammatory growth.
IV	M.	33	Persistent vomiting due to vicious circle.
V	F.	16	Exhaustion, persistent postoperative diarrhea.
VI	F.	5	Bronchopneumonia following one day after operation in a weakened patient; death on fifth day.
VII	M.	1	Bronchopneumonia in a very weak man.

The results of gastroenterostomy during the first year of the operation are fairly satisfactory. Of the 100 cases operated on, 7 had died immediately following operation, and the results of 16 could not be obtained; the results are therefore tabulated in only 77 cases, consisting of 43 males and 34 females; the results were entirely satisfactory in 34 males and 31 females, that is in 65 instances (84.4 per cent.), and unsatisfactory in 9 males and 3 females, that is in 12 instances (15.6 per cent.).

RESULTS OF OPERATION DURING FIRST YEAR.

	Males.		Females.	
Age.	Satisfactory.	Unsatisfactory.	Satisfactory.	Unsatisfactory.
20 to 30 years	4	1	5	1
30 to 40 "	8	1	9	1
40 to 50 "	12	4	7	0
50 to 60 "	8	1	9	1
60 to 70 "	2	2	1	0
Total	34	9	31	3

Of the total of 100 cases the final results of 19 are unknown while 7 died soon after operation, leaving 74 cases. Of these the results were satisfactory in 32 males and 29 females, that is, 61 (84.2 per cent.) and unsatisfactory in 8 males and 5 females, that is, 13 (15.8 per cent.).

RESULTS AFTER FIRST YEAR OF REMAINING SEVENTY-FOUR CASES.

	Males.		Females.	
Age.	Satisfactory.	Unsatisfactory.	Satisfactory.	Unsatisfactory.
20 to 30 years	3	1	1	1
30 to 40 "	8	2	8	2
40 to 50 "	11	3	7	0
50 to 60 "	8	1	9	1
60 to 70 "	2	1	1	1
Total	32	8	29	5

In the following table are noted the number of cases that have been observed from one to eleven years after operation together with the final results. The average of the satisfactory recoveries is shown to be 84.2 per cent. If we deduct from this number 7 per cent. that those cases already referred to, in which death occurred immediately upon operation, the percentage of favorable results is reduced to 77.2 per cent.

In a series of Roentgen-ray plates made in four cases, all of which had been operated on over a year, it was demonstrated that while in most instances the gastroenterostomy opening was functioning quite normally a portion of the gastric contents continued to empty itself through the pylorus.

End Results in Years after Operation of Gastroenterostomy.

Years.	Total No. of cases.	Satisfactory results.	Unsatisfactory results.	Percentage of satisfactory recoveries.
1	9	8	1	88.8
2	5	5	0	100.0
3	8	7	1	87.5
4	7	6	1	85.7
5	4	3	1	75.0
6	7	5	2	71.4
7	5	5	0	100.0
8	9	9	0	100.0
9	7	6	1	85.7
10	8	6	2	75.0
11	5	3	2	60.0
Average of percentage of satisfactory recoveries				84.2
Deaths				7.0
Favorable results				77.2

Fom our observations of a study of 100 cases of gastroenterostomy we believe we are justified in arriving at the following conclusions:

1. The largest proportion of cases in our series in which gastroenterostomy was performed occurred between the thirtieth and sixtieth years, while the largest proportion of cases in which pyloroplasty was performed occurred between the thirty-fifth and fiftieth years.

2. Of the total number of cases of gastroenterostomy there were 56 males and 44 females, while the total number in the pyloroplasty series numbers 63 males and 37 females.

3. The duration of the symptoms in our gastroenterostomy cases varied from one month to nineteen years, the average duration being nine and a half years, while the duration of symptoms in our pyloroplasty cases varied between one and one half months to twenty-five years, the average duration being nine and a half years.

4. In the gastroenterostomy cases the symptoms appeared in the following proportions: pain 90 per cent. (51 males and 39 females); vomiting in 65 per cent. (36 males and 29 females); hematemesis in 23 per cent. (18 males and 5 females); melena in 44 per cent. (28 males and 16 females); retention in 36 per cent. (19 males and 17 females); while in the pyloroplasty cases pain was present in 92 per cent. of cases (58 males and 34 females); vomiting in 64 per cent. (44 males and 20 females); hematemesis in 21 per cent. (15 males and 6 females); melena in 46 per cent. (29 males and 17 females); retention in 42 per cent. (27 males and 15 females).

5. In the gastroenterostomy series the ulcer cases are arranged as follows: there are 46 cases of gastric ulcer (32 males and 14 females), 38 duodenal ulcers (15 males and 23 females), making a total of 84 cases. In the pyloroplasty cases there were 55 cases of gastric ulcer (36 males and 19 females) and 32 duodenal ulcers (21 males and 11 females, making a total of 87 cases. It will be noted that in both series there is a preponderance of males over females, and of gastric over duodenal ulcers.

6. In 67 of the gastroenterostomy patients operated on for obstruction 44 were due to gastric ulcer, 14 to duodenal ulcer, and 9 to adhesions, while pyloroplasty was performed for obstruction in 64 instances; for gastric ulcer in 51, for duodenal ulcer in 7, and in 6 for adhesions.

7. In our gastroenterostomy cases secondary operations were performed in four instances to correct immediate difficulties while in the pyloroplasty cases secondary operations were required in the same number of instances for a similar purpose.

8. After gastroenterostomy satisfactory results were secured in 82 per cent. of cases, and unsatisfactory in 18 per cent., while pyloroplasty was immediately successful in 90 per cent. cases and unsatisfactory in 10 per cent.

9. There were seven deaths, following immediately upon the operation of gastroenterostomy, while but five deaths followed pyloroplasty.

10. Of the 77 cases of gastroenterostomy followed during the first year of the operation the results were satisfactory in 84.4 per cent. and unsatisfactory in 15.6 per cent., while of the 82 cases of pyloroplasty the results were entirely satisfactory in 93.9 per cent., and unsatisfactory in 6.1 per cent.

11. Of the gastroenterostomy cases numbering 74 followed after the first year of operation, the results were satisfactory in 84.2 per cent., and unsatisfactory in 15.8 per cent., while of the pyloroplasty cases numbering 78, the results were satisfactory in 93.6 per cent., and unsatisfactory in 6.4 per cent.

12. The end results in the gastroenterostomy cases showed a percentage of 77.2 per cent. of satisfactory recoveries, while the pyloroplasty cases showed a percentage of 88.6 per cent.

It is quite evident from our study of 100 gastroenterostomy operations and from a similar number of pyloroplasties that the immediate as well as the final results are clearly in favor of pyloroplasty. The only indications in favor of gastroenterostomy are, as we have already pointed out, in those instances in which there is an inability to mobilize the duodenum when adhesions are too dense, and in those cases in which there is a thickening and infiltration about the pylorus due to hypertrophic ulceration, conditions, however, which in our experience occur but rarely. Again there is no possibility of excising the ulcers when performing gastroenterostomy, as can frequently be accomplished in pyloroplasty, when they are in the anterior wall.

While in some instances gastroenterostomy may be the operation of choice, nevertheless we believe that on account of its comparative unsatisfactory end results, it should be as far as possible limited to the relief of stenosis of the pylorus, due to malignant disease, and that usually in nearly all other conditions pyloroplasty and pylorectomy are safer and more satisfactory procedures.

PROLONGED FASTING IN DIABETES.[1]

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Partial pancreatectomy, with preservation of the pancreatic duct so as to avoid atrophy of the remnant, gives a more satisfactory reproduction of clinical diabetes than is afforded by von Mering and Minkowski's total pancreatectomy or Sandmeyer's method of slow pancreatic atrophy. Simple lowering of the sugar tolerance without diabetes, or diabetes varying in intensity from the mildest to the very severe, can thus be produced at will. As previously pointed out,[2] animals thus prepared constitute valuable test-objects and afford favorable opportunities for research concerning diabetic therapy. In the milder types the measures ordinarily used in human diabetes, namely, restriction of carbohydrate or protein and brief fasting, if necessary, suffice to keep the animals sugar-free and in good condition indefinitely. But in a more severe type these measures do not suffice and the animal quickly passes into a hopeless condition if more radical treatment is delayed. In this type the initial fast must sometimes be measured in weeks rather than in days. The subsequent diet must be such as to keep the animal at a low level of weight and metabolism. Certain influences which increase either weight or metabolism tend to bring back glycosuria in these animals as in human patients. If glycosuria persists in any animal the result is a downward sequence of lowered tolerance, emaciation, weakness, cachexia, and death, with parallel degenerative changes in the islands of Langerhans. If glycosuria is prevented, the animals may remain lively and strong though thin; they may improve somewhat with time, and the islands seem to be spared. This evidence supports the hypothesis that one set of influences overtax and injure the internal function of the pancreas, and the opposite set of influences protect and rest the internal function of the pancreas.

The treatment of diabetes at the Rockefeller Hospital has been based upon these animal experiments. The patients admitted have been forty-four, chosen as the most severe out of a considerable number of applicants, and representing a sufficient variety as respects age, social condition, and other factors. Certain points may here be mentioned concerning (1) the initial fast and (2) the subsequent diet.

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[1] Read at the meeting of the Association of American Physicians, Washington, D. C., May, 1915.

[2] Allen, F. M., Studies Concerning Glycosuria and Diabetes, Harvard University Press, Cambridge, Massachusetts.

Fasting has been employed by writers from Naunyn to Guelpa. The same writers describe a numerous class of diabetics who are not made sugar-free, but go on with glycosuria and acidosis and die in coma. Other patients are made sugar-free only after months of strict dietary treatment, including occasional single or repeated fast-days. Present experience indicates that the glycosuria in cases of even the severest type of diabetes may with advantage be cleared up by one initial fast. The necessary duration may sometimes be as long as eight or ten days. In one case of maximum severity in a youth, aged seventeen years, the changes accompanying fasting were studied by Dr. Eugene Du Bois in the respiration calorimeter. He found that at the outset the total metabolism was about 8 per cent. above normal and the patient was excreting all or nearly all of the sugar formed from protein and burning practically no sugar at all. In a nine days fast the glycosuria ceased, the total metabolism fell to about 20 per cent. below normal, and the respiratory quotient showed that the sugar formed from protein was being burned. It will be remembered that respiratory quotients in the most severe cases during the "oat cure" do not show increased combustion of carbohydrate. The above metabolic observations are new and constitute important evidence for the functional element in the etiology of human diabetes, since they show to what extent recovery can take place within a few days when the most complete possible rest is given the weakened metabolic function.

Severe acidosis, which is known to be diminished by the shorter fasts previously employed, is still more reduced by the more prolonged fasting. Dangerously weak and emaciated patients have borne the fasting with apparent benefit, giving the impression that they had been suffering more from intoxication than from lack of nutrition. Alcohol is valuable during fasting as a food which does not produce glycosuria, though its use is not essential. Broadly speaking, freedom from glycosuria seems attainable in all cases of uncomplicated human diabetes before there is danger of death from starvation. In a few cases seen personally or described by others, death from some severe complication has occurred before the urine became sugar-free. In such cases to date the complication has been a severe infection, or some condition strongly tending to increase metabolism or produce nervous or circulatory disturbance. The fasting has not appeared harmful even in these few cases where it has not been successful. One case of incipient gangrene and one dangerous carbuncle cleared up rapidly under fasting, and threatening complications of infectious or any other character are considered an indication for the radical treatment as described. No contraindication has been met, unless it be the appearance of nausea, vomiting, and prostration while fasting. One woman died in such an attack; but there were attacks of this character in her previous history, and it is not positive that either the attack or the death was due to the fasting. One man began to vomit and feel unwell on the seventh day of fasting. He was fed and the symptoms immediately passed off. After two weeks of restricted diet a second fast easily cleared up the glycosuria. This simple precaution apparently prevents danger even in this rare type of cases, and in other cases there has never been any sign of danger or harm.

Though the initial fast, to clear up glycosuria and other symptoms, is generally a very simple matter, the subsequent diet, to maintain this condition, is sometimes difficult. It is unquestionably true, in accord with Joslin's[3] warning, that when glycosuria is abolished and strength diminished by long fasting, and then glycosuria and acidosis allowed to return through improper diet, the last state of that man may be worse than the first. Herein may be found the causes of failure in past attempts of this sort. After the fasting patient has been completely sugar-free for one or two days, feeding is begun as outlined in former papers,[4] and the tolerance of the patient for carbohydrate, protein, and fat is determined. Just as fasting is continued not for any limited number of days, but as long as necessary for sugar-freedom, so also the diet is governed not by any theoretical standard of protein or calories, but by the amount of each food that can be given in each individual case while keeping the urine clear. Under this program even weak and emaciated patients have been subjected to under-nutrition in both protein and calories for weeks or months continuously, with ultimate benefit. Any trace of glycosuria is the signal for a fast-day with subsequent modification of diet, and routine fast-days are often used as frequently as once a week even in absence of glycosuria. While individual details must be reserved to a later publication, two principles in the management of severe cases may be mentioned, namely, the benefit of keeping the patient permanently below weight, and the advisability of restricting the quantity of fat in the diet.

A slight temporary reduction of weight was practiced in some cases by Naunyn, whose example has been widely followed. This was not carried to the point of abolishing glycosuria and acidosis in the severest cases; and generally the attempt has been to maintain these patients at the highest possible level of weight and nutrition, with the idea of helping them to withstand a wasting disease. The present idea is the opposite to this, namely, that the reduction of weight is in itself beneficial to the diabetic condition and serves to spare the weakened function and increase tolerance. This measure, like the others, is carried to any point that may be necessary in any particular instance. Sometimes a slight reduction of weight suffices even for a severe case. Again, a well-nourished patient, easily kept free from glycosuria, was reduced by twenty kilograms merely because of a slight stubborn ketonuria and a persistently high blood-sugar. Most patients are able to regain weight to a greater or less extent, but few severe ones are able to return fully to normal weight. Any increase that is possible without return of symptoms is permitted. Any gain that brings back glycosuria or ketonuria is checked. The experience in human patients thus far runs parallel to that in the animal experiments upon which this suggestion was founded.

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[3] Discussion of paper at meeting of Suffolk County Medical Society in connection with Boston Medical Library, December 2, 1914.

[4] Allen, F. M., Jour. Amer. Med. Assoc., September 12, 1914; Boston Med. and Surg. Jour., February 18, 1915.

In the treatment of diabetes heretofore, fat has been freely given and even forced upon the patient. It has been restricted only in certain cases with high acidosis and danger of coma. The doctrine has been that fat does not affect diabetic glycosuria except in very rare "fat-sensitive" patients; also, that the diabetic must receive the number of calories required by his metabolism, plus the number of calories lost as sugar and acetone bodies in the urine, and fat has been considered the best food for crowding in these calories. Anyone can readily convince himself that, in a suitably severe diabetic who is symptom-free for days or weeks on a fixed diet, the addition of some quantitiy of butter or olive oil to the diet will bring back the glycosuria, ketonuria, and other symptoms immediately or within a short time. The feeding of fat alone does not cause glycosuria, and there is no proof that the sugar is formed from the fat; more probably the sugar excretion results from the stimulating effect of fat upon metabolism. The overtaxing of the patient's metabolism by giving fat beyond the limit of tolerance may be an additional explanation of the failure to keep certain patients free from glycosuria and ketonuria under former methods of treatment.

Concerning any proposed treatment, inquiry is proper whether it is new and whether its results are superior to those of the old methods. The following statements can be made regarding these points.

The principle tentatively suggested that increase of weight or metabolism increases strain upon the internal pancreatic function and reduction of weight or metabolism reduces strain upon the internal pancreatic function, is new, and if it proves valid will be a useful general guide in treatment. The animal experiments likewise are entirely new. The general policy of insisting upon prompt and lasting freedom from glycosuria and acidosis in all cases of diabetes, even the severest, is a new one. In addition, the main features wherein the proposed treatment differs from the previously established methods may be summarized under the following five headings. The first two represent differences merely of degree, in that the proposed treatment is more radical than the old; namely, first, an initial fast sufficient to clear up glycosuria in any case and then one or two days longer; second, a subsequent diet such as to keep glycosuria and acidosis permanently absent, with as many interspersed fast-days as necessary for this purpose. The third and fourth features represent differences not in degree but in kind, and are diametrically opposed to the prevalent teachings; that is, the third opposes the idea that the diabetic should be kept at the highest possible level of weight and strength, and that gain in weight is synonymous with improvement; and it substitutes for this the plan of keeping most severe diabetics intentionally and permanently at a sufficiently low level of weight and metabolism, in the belief that return of symptoms and downward progress is thus prevented. The fourth feature stands opposed to the doctrines that fat feeding does not appreciably influence diabetic glycosuria, and that calories lost in the urine should be replaced by additional calories in the diet, preferably in the form of fat. It opposes to these the observation that addition of fat to a fixed diet suffices to bring back both glycosuria and ketonuria in most severe diabetics, and the principle that the patient's tolerance for fat and calories should be followed in the same way as the tolerance for carbohydrate and protein. The fifth feature consists merely of routine or incidental matters, which are not without practical importance. Among these may be mentioned (1) the diet such as not to overtax tolerance and yet satisfy the patient sufficiently that he will follow it continuously at home; (2) the absence of any specific craving for carbohydrate such as diabetics are supposed to manifest, and the contradiction of the prevalent idea that most severe diabetics cannot be trusted; (3) the avoidance of the need of alkali for more than a few days, and therewith relief from disturbances due either to acidosis on the one hand or to prolonged large doses of soda on the other; (4) the principle of clearing up the urine quickly and devoting the greater part of the stay in hospital to educating the patient, rather than devoting the greater part of the stay in hospital to clearing up the urine and dismissing the patient shortly thereafter; (5) instruction of the patient in the simple means of controlling his own condition, through his diet, his body weight, and the daily testing of his own urine with Benedict's solution.

The immediate results as observed up to the present have appeared uniformly beneficial. Reports from a number of clinicians experienced in the older methods of treating diabetes agree that these results under the new method are more favorable. Also the relative simplicity of the proposed method, and the fact that it stops glycosuria without running any risk of acidosis, makes it available for a large body of general practitioners who have heretofore not felt safe in withdrawing carbohydrate or attempting to stop glycosuria in cases with any marked ketonuria. Patients also generally accept radical treatment with quick decisive results more readily than the weeks or months of privation heretofore used in stopping glycosuria, and the quick relief from polyphagia, polydipsia, and other symptoms aids further in securing their coöperation. For these reasons it is believed that the innovations described are of some real value. As respects the remote results and the influence on the ultimate prognosis of severe diabetes, longer experience must decide. A question is here involved whether diabetes is an inherently progressive disease or whether it is the simple weakness of a metabolic function. If it is the former, patients must ultimately go down hill and die, though not in diabetic coma, and the benefit will consist only in lengthening their lives and keeping them more comfortable. If it is the latter, downward progress may be indefinitely prevented by avoiding overstrain of the weak function, just as in animals. Among the patients treated thus far, during a variable number of months in the hospital and at home, spontaneous downward progress has not yet been observed. Whatever the ultimate outcome, two conclusions seem justified by present knowledge: (1) that this treatment removes glycosuria and acidosis more quickly and surely than has been the practice heretofore, and (2) that patients do better when glycosuria and acidosis are removed than when they are allowed to continue.

PRESENT-DAY TREATMENT AND PROGNOSIS IN DIABETES.

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It is no exaggeration to say that the advance in the actual treatment of diabetes mellitus during the twelve months just passed has been greater than in any year since Rollo's time, and it should be emphasized that this improvement in treatment comes not by chance, but as a result of patient scientific experimentation, which has been based upon the work of the foremost investigators in both laboratory and clinic. It follows experiments upon animals, and is an answer to those critics who have claimed that animal experimentation in diabetes had failed to justify itself. At the same time better and simpler technical methods for the study of the blood, urine and respiratory exchange, as well as new knowledge of the metabolism of diabetes, have contributed a share to this improvement. The truthfulness of the foregoing is easily shown. One year ago physicians were generally afraid to teach their patients to test their urines for sugar; today the physician feels himself to so much greater an extent master of the disease that this is one of the first steps to be taken.

The advantage of maintaining the urine sugar-free has been universally recognized, but all have conceded that this was impossible without danger from acidosis and inanition. Fasting and a low diet have been known, but it is only fair to give Allen the credit of first to see the therapeutic significance of inanition upon a severe case of diabetes, second to prove upon diabetic dogs that prolonged fasting would render them sugar-free, and third to have the courage of his convictions and apply this principle to human diabetes. Thanks to Dr. Frederick M. Allen we no longer nurse diabetics—we treat them!

A review of all my private cases of diabetes, undertaken for this special purpose, has convinced me that prolonged fasting has produced results far and away ahead of any methods which I have hitherto employed. For myself, I consider the impression which I have thus obtained of far more value than any statistics which my records afford, but it is almost my duty to present these as well.

TABLE I.—CASES UNDER OBSERVATION MAY 1, 1914, TO MAY 1, 1915.

Cases.	Total.	Traced.	Dead.		Alive.	
			No.	Per cent.	No.	Per cent.
Total	211	211	31	14.7	180	85.3
Old	75	75	11	14.7	64	85.3
New	136	136	20	14.7	116	85.3
Fasted	55	55	6	10.9	49	89.1
Not fasted						

Old cases are those first seen prior to May 1, 1914; new cases are those first seen after May 1, 1914.

TABLE II.—AGE AT DEATH OF FATAL CASES.

Cases.	Total.	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80
Old	11	0	1	0	1	2	2	1	4
New	20	3	2	3	0	3	6	1	2

As a matter of fact, I have seen 211 cases (75 old and 136 new) of diabetes in the twelve months from May, 1914 to May, 1915. All of these have been traced and are available for statistics. (See Tables I and II.) Of these 13 are dead, a mortality of 15 per cent. Fifty-five of the 211 cases were fasted and of these 6 died—a mortality of 11 per cent. In this paper I will discuss the causes of death of fatal cases among the number fasted. Case No. 648 was the first case I fasted, and I simply kept her sugar-free a part of one day in May, and then allowed her gradually to return to her former diet. She died in coma June 16, 1914. Case No. 707 was my second case to undergo fasting, and he never actually became sugar-free. He at once returned home, broke all dietetic restrictions, and died in forty-six days of coma. I had not then gained sufficient confidence in the treatment to impart it to the patients and to prevail upon them to carry it through to the end. Today there is no need of that, for one patient laughs the other half through the fasting days. Another death was Case No. 855, aged seventy years, onset at fifty-eight years, weight 220, who was first seen by me four days after an operation for appendicitis, during which, unfortunately, a large quantity of ether was employed. Despite fasting, which for the most of the time had been nearly absolute, he never became sugar-free. He died of heart failure, without coma, but probably associated with a necrosis of the cells of the liver and pancreas. Case No. 764 was fasted after leaving my supervision by another physician. The patient broke treatment, exercised unusually, and died promptly in coma. He lived some four hundred miles from Boston, and seven miles from the physician in attendance, and was that physician's first case. Case No. 576 was fasted. He died of recurrence of cancer in the scar of the abdominal incision forty-seven days after the growth had been removed from the bladder by Dr. Chute. Case No. 430, who developed diabetes in June of 1908, at the age of fifty-two years, came under my observation in July, 1911, and was fasted for a day in September, 1914. He returned to Canada and died on March 12, 1915, of diabetic coma. The other 49 cases which have been fasted are alive.

Corroborative evidence of the value of Dr. Allen's ideas is the gratifying fact to me that the last death to occur while the patient was under my personal supervision in a hospital was on August 29, 1914. That patient, Case No. 758, had a blood-pressure of 215, and died of coma. Since that date 48 cases have been treated by me in hospitals without a death.

The study of the respiratory quotient of two groups of fatal cases of diabetes and another group of living cases furnishes evidence which is worthy of mention. These investigations were made at the Nutrition Laboratory of the Carnegie Institution in conjunction with Professor Francis G. Benedict, and are illustrated in Tables III and IV. In the first group of fatal cases with a respiratory quotient of 0.71, the duration of life following the period of observation varied between forty-four and fourteen days. In another group of eight fatal cases with the somewhat higher respiratory quotient of 0.74, the duration of life under similar conditions varied from four hundred and forty-two to seventy days. In comparison with these groups of fatal cases, there is a group of four cases still living. The average respiratory quotient of these four cases was 0.715, but the duration of life had already reached, up to May 1, 1915, from eight hundred and sixty-two to one hundred and thirty-four days. These patients are now (June 1, 1915) all alive and are in good condition. Furthermore, they have been treated along lines employed by Dr. Allen.

TABLE III.—RESPIRATORY QUOTIENT IN SEVERE DIABETES.

Year.	Cases.	Observers.	R. Q.
1894	1	Weintraud and Laves	0.70
1897	2	Nehring-Schmoll	0.72
1905	2	Magnus-Levy	0.71
1907	1	Mohr	0.72
1908–1911	19	Benedict and Joslin	0.73
1912	8	Rolly	0.74
1912	3	Grafe and Wolf	0.74
1912–1914	7	Benedict and Joslin	0.73

TABLE IV.—RESPIRATORY QUOTIENT IN FATAL AND LIVING CASES OF SEVERE DIABETES COMPARED.

Fatal cases.			Four living cases.		
No. of cases.	Days before coma.	R. Q.	Case number.	Days before May 1, 1915	R. Q.
6	44–14	0.71	552	862	0.72
			765	187	0.73
			786	173	0.71
8	442–70	0.74	806	134	0.70
			4 cases	862–134	0.715

The behavior of the various types of diabetes under fasting and a low diet is not quite uniform. The mild and moderately severe cases have done well and time has been saved in the initial treatment. A good many of the moderately severe cases, who frequently showed sugar, now keep sugar-free easily and this has contributed much to their peace of mind. Both conditions may be attributed to the patients having learned to test their own urines. Children have been particularly favorable subjects, although I cannot say that I have a case under treatment which has exceeded that of Case No. 74, a duration of three years and eleven months, which is my record case for a child with an onset under fifteen years.

Complications of pruritus, carbuncles, and abscesses have cleared up better than formerly, and so did one case with neuritis. A woman, Case No. 812, six months pregnant and with 6.4 per cent. of sugar, under a low diet—not fasting—became sugar-free, was delivered by Cesarean section by Dr. J. C. Hubbard, and both baby and patient are now, eight weeks later, in good condition. Other patients have been operated upon successfully for cancer of the uterus, cancer of the bladder, removal of prostrate, amputation for gangrene and for extensive carbuncles.

The results are divergent with long-standing cases. In one notable case, Case No. 801, of ten years' duration, there is no question but that the improvement has been marked, and now he lives comfortably on a diet of 45 grams carbohydrate or less and attends to his customary occupation. Incidentally, the recovery from a carbuncle which led to his first coming to me for treatment, was unusually prompt. But another case, Case No. 352 of twenty-one years' duration, who was not doing well, although he has become sugar-free, has a tolerance of only 10 to 15 grams carbohydrate. His weight is maintained after an initial loss of four and one-half pounds, but he is weak. I think that his strength will return, but the blood sugar varies between 0.14 per cent., 0.19 per cent. and 0.27 per cent., although no complicating nephritis is present.[1] Another patient, Case No. 664, has steadily lost weight and although she feels fairly comfortable, is weak. Perhaps I should treat this last patient more rigorously—perhaps the diseased pancreatic function is really becoming exhausted. Sometimes it almost seems as if a patient with diabetes, as well as his friends, felt injured if his span of life was not prolonged further than that of a healthy individual. There is no question but that many of the patients of a severe type are less vigorous for some weeks after the fasting period is over than before it began, when they were excreting sugar. In a number of cases time enough has elapsed to show that strength is regained, but this is not universal Perhaps I look for too quick results. However, it would not be fair to say to an active diabetic doctor, with a rather severe type of diabetes, that if he followed this plan of treatment he could return to a strenuous practice in three or four weeks. Of course he ought not to have a strenuous practice, but all of us know that many such physicians do. On the other hand, it would be perfectly correct to say, if you follow this plan of treatment, there is little doubt but that you will live longer, only you must live at a reduced rate.

There remains the type of disease with severe acidosis, and for these patients this form of treatment is almost universally successful. Table V on page 490 illustrates this point.

Unfortunately, in none of the severe cases has there been any decided gain in tolerance, although there have been deceptive apparent gains.

The advantages of the new treatment are many. It has made attainable the ideals of treatment—namely, a sugar-free and acid-free urine. The standards of the success of treatment are so simple that they are within reach of the patient. At one stroke the patient is delivered from medicines, patent and otherwise, sham kinds of treatment, gluten breads, and in 99 cases out of 100 of alkalis. He can now test all measures for himself. Consider the amount of time and money saved both doctor and patient in urinary tests.

The hospital stay is not particularly shortened, except indirectly by the avoidance of complications, because the patient requires a more thorough education in the diet. It does simplify general hospital treatment, because so soon as a diabetic patient in an open ward shows sugar, it will generally mean that he has broken his diet, for which the automatic penalty is a fast until sugar-free.

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[1] This patient has continued to improve, looks well and rides horseback. July, 1915.

TABLE V.—CASE NO. 740. MALE. ONSET IN MAY, 1914, AT TWENTY YEARS AND TEN MONTHS.

Date 1915	Body weight.	Volume of urine.	Reaction.	Total nitrogen.	NH_3-N	Acetone and diacetic acid.	Diacetic acid (Qual.)	Beta-oxybutyric acid.	Dextrose (Grav.)	Diet.					Blood sugar.	Alveolar air CO_2 tension.	CO_2 per kilo per min.	O per kilo per min.	R. Q.	Calories per kilo per 24° from O_2.
										Carbohydrate	Protein.	Fat.	Alcohol.	Calories.						
	Kilos.	c.c.		gms.	gms.	gms.		gms.	gms.	gms.	gms.	gms.	gms.	gms.	%	m.m.	c.c.	c.c.		
March 27	54.0	3000	Acid	32.70	5.60	..	++++	..	74											
April 14–15 (14¼ hrs.)	52.9	1430	Acid	12.44	2.61	3.11	+	19.99	40	..	..	..	0							
" 15–16	52.2	1540	Acid	16.48	3.16	3.70	+	18.33	39	13	50	70	0	882	0.26	24.1	2.91	4.06	0.72	27.5
" 16–17	51.7	1420	Acid	16.20	3.28	3.09	++	13.41	45	17	55	75	0	963	0.43	29.5	3.02	4.15	0.73	28.2
" 17–18	52.1	900	Acid	9.63	2.44	2.00	+	8.23	16	0	7	0	24	196	0.26	31.4	2.93	4.08	0.72	27.6
" 18–19	51.7	680	Acid	8.10	2.14	1.79	++++	7.85	8	0	6	0	0	24	0.33	31.0	2.84	3.87	0.73	27.0
" 19–20	50.6	580	Slightly acid	6.80	1.73	1.29	+++	5.59	3	0	0	0	24	168	0.29	31.6	2.84	3.76	0.76	25.7
" 21–22	51.5	540	Slightly acid	7.90	1.57	1.18	++	4.40	0	0	5	0	24	188	0.23	32.1	2.71	3.61	0.75	24.6
" 24–25	51.6	570	Acid	9.10	1.57	1.09	+++	3.55	0	5	20	25	18	451	0.31	30.8	2.61	3.54	0.74	24.1
" 27–28	50.9	640	Slightly acid	7.40	1.02	0.91	+	3.10	Trace	0	2	0	15	113	0.31	..	2.73	3.67	0.75	25.0
May 1.	50.4	945	Slightly acid	7.60	0.74	0.83	0	2.64	Trace	0	2	0	15	113	0.28	32.9	2.61	3.44	0.76	23.5

Unquestionably complications will become less frequent, and it is possible that arteriosclerosis will less commonly occur in the long standing cases as a result of the restricted diet.

One of the greatest benefits which will be derived from the new method of treatment is the basis which it will give for new lines of experimental work. The question of the D : N ratio should be soon settled. Already new facts have appeared as a result of the study of the metabolism of these patients, and to some of these attention is now directed.

The investigation of the metabolism of severe cases of diabetes has been continued by Professor Benedict and myself at the Carnegie Laboratory, and 19 more patients have been studied since September 1, 1914. The first notable change which we observed was an upward tendency of the respiratory quotient in these cases following the institution of a fast. This became so marked that we had doubts about the accuracy of the respiration apparatus which we employed. A new apparatus, devised by Dr. Benedict, but not yet described, was also employed, and with this the results were essentially the same. Still more recently we have confirmed our data with the Tissot apparatus and the bed calorimeter. In January we compared the results which Dr. Du Bois obtained with two of Dr. Allen's patients, and noted that in his laboratory a similar tendency had been recorded. Table V illustrates this increasing respiratory quotient and other changes in the metabolism. The patient was Case No. 740, a young man in whom the onset of the disease occurred at the age of twenty years and ten months in 1914. He showed, nineteen days before the first test, 5.6 grams of ammonia nitrogen in twenty-four hours, and 74 grams sugar in the urine upon a diet supposedly containing but a few grams of carbohydrate. In June he was sugar-free and at work.

It will be noted that the respiratory quotient was 0.72 upon the first day of observation, but gradually rose to 0.76 upon the last day. If one calculates the non-protein respiratory quotient, it will be seen that this also rose, and it is obvious that notable quantities of carbohydrate, or some material with a high respiratory quotient, must have been burned following the starvation treatment. This remarkable phenomenon is hard to explain. Has the diabetic patient actually more carbohydrate in the body than is commonly supposed? Could the rising quotient be due to combustion of acid products, of which the respiratory quotients for acetone, diacetic acid and beta-oxybutyric acid are 0.75, 1 and 0.89 respectively? The chart shows that if a diabetic is fasted acidosis disappears, and this is in marked contrast to the behavior of normal men, for they present acidosis upon fasting with no increase in the respiratory quotient as the fasting proceeds.

The metabolism at the beginning of the experiment was 18 per cent. higher than at the end. Coincident with this decrease in the metabolism was the fall in acidosis. It appears, furthermore, logical to conclude that if the metabolism had been estimated a few days prior to the first experiment when the acidosis was greatest of all, amounting to 5.6 grams ammonia-nitrogen, the metabolism would have been still greater. The normal metabolism for this patient lay probably somewhere between the metabolism first and last recorded, and one would not be far wrong to estimate it at the beginning of the test at 10 per cent. above normal and at the end at 10 per cent. below normal. The significance of the fall in metabolism with the decrease in acidosis is striking.

The chart is also instructive in that the falling metabolism bears no relation whatsoever to the blood sugar, for this was essentially the same throughout. It is interesting that the calories per kilo per twenty-four hours, as calculated from the oxygen inhaled, amounted to approximately 28 to 24 per day, and that the calories given the patient during the latter part of the period were approximately this same figure. Subsequent days have confirmed the observation that this patient, when sugar and acid-free, can hold his weight at a little less than 30 calories per kilogram body weight.

The method which has been employed in the treatment of these cases has been similar to that recommended and described by Dr. Allen. The more closely his directions have been followed the better the patients have done. No patient has required more than five days to become sugar-free. Many patients became sugar-free after the omission of three or four meals. Patients are put to bed and the plan of treatment is carefully explained to them. They are furnished with note-books in which answers to their questions are recorded, taught the use of a diet card and how to examine the urine for sugar with Stanley R. Benedict's solution. As a working basis the general plan of treatment is summarized below, and for convenience the following diet chart, printed on a card five by three inches, has been used.

FASTING. Fast until sugar-free. Drink water freely and one cup tea and one cup coffee if desired. If sugar persists after two days of fasting, add in divided portions 300 c.c. clear meat broth.

ALCOHOL. If acidosis (diacetic acid) is present, take 0.5 c.c. alcohol per kilogram body weight daily until acidosis disappears. Alcohol is best given in small doses every three hours.

CARBOHYDRATE TOLERANCE. When the twenty-four hour urine is sugar-free, add 150 grams of 5 per cent. vegetables, and continue to add 5 grams carbohydrate daily up to 20 grams, and then 5 grams every other day, passing successively upward through the 5, 10 and 15 per cent. vegetables, 5 and 10 per cent. fruits, potato and oatmeal to bread, unless sugar appears or the tolerance reaches 3 grams carbohydrate per kilogram body weight.

Strict Diet. Meats, Fish, Broths, Gelatine, Eggs, Butter, Olive Oil, Coffee, Tea and Cracked Cocoa.

Foods Arranged Approximately According to Per Cent. of Carbohydrates.

5 per cent.		10 per cent.	15 per cent.	20 per cent.
VEGETABLES				
Lettuce	Cauliflower	Onions	Green peas	Potatoes
Spinach	Tomatoes	Squash	Artichokes	Shell beans
Sauerkraut	Rhubarb	Turnip	Parsnips	Baked beans
String beans	Egg plant	Carrots	Canned lima beans	Green corn
Celery	Leeks	Okra		Boiled rice
Asparagus	Beet greens	Mushrooms		Boiled macaroni
Cucumbers	Water cress	Beets		
Brussels sprouts	Cabbage			
	Radishes			
Sorrel	Pumpkin			
Endive	Kohl-rabi			
Dandelions	Broccoli			
Swiss chard	Vegetable marrow			
Sea kale				
FRUITS				
Ripe olives (20 per cent. fat)		Lemons	Apples	Plums
Grape fruit		Oranges	Pears	Bananas
		Cranberries	Apricots	
		Strawberries	Blueberries	
		Blackberries	Cherries	
		Gooseberries	Currants	
		Peaches	Raspberries	
		Pineapple	Huckleberries	
		Watermelon		
NUTS		Brazil nuts	Almonds	Peanuts
Butternuts		Black walnuts	Walnuts (English)	
Pignolias		Hickory	Beechnuts	
		Pecans	Pistachios	40 per cent.
		Filberts	Pinenuts	Chestnuts

MISCELLANEOUS

Unsweetened and unspiced pickles, clams, oysters, scallops, liver, fish roe

Reckon *actually available* carbohydrates in vegetables of 5 per cent. group as 3 per cent., of 10 per cent. group as 6 per cent.

Contain approximately.	Protein.	Fat.	Carbohydrates grams.	Calories.
Oatmeal, dry weight	5	2	20	110
Meat (uncooked)	6	2	0	40
Meat (cooked)	8	3	0	60
Broth	0.7	0	0	3
Potato	1	0	6	30
Bacon (cooked)	5	15	0	155
Cream, 40 per cent.	1	12	1	120
Cream, 20 per cent.	1	6	1	60
Milk	1	1	2	20
Bread	3	0	18	90
Butter	0	25	0	240
Egg (one)	6	5	0	75
Brazil nuts	5	20	2	210
Orange (one)	0	0	10	40
Grape fruit (one)	0	0	10	40
Vegetables, 5-10 per cent. groups	0.5	0	1	6

1 gram protein, 4 calories.
1 gram fat, 9 calories.
6.25 grams protein contain 1 gram nitrogen.
30 grams (g) or cubic centimeters (c.c.) = 1 ounce.
A patient "at rest" requires 25 to 30 calories per kilogram body weight.
1 gram carbohydrate, 4 calories.
1 gram alcohol, 7 calories.
1 kilogram = 2.2 pounds.

Protein Tolerance. When the urine has been sugar-free for two days, add 20 grams protein (three eggs) and thereafter 15 grams protein daily in the form of meat until the patient is receiving 1 gram protein per kilogram body weight, or if the carbohydrate tolerance is zero, only $\frac{3}{4}$ gram per kilogram body weight. Later, if desired, the protein may be raised to 1.5 gram per kilogram body weight.

Fat Tolerance. While testing the protein tolerance, a small quantity of fat is included in the eggs and meat given. Add no more fat until the protein reaches 1 gram per kilogram (unless the protein tolerance is below this figure), but then add 25 grams fat daily until the patient ceases to lose weight or receives not over 40 calories per kilogram body weight.

Reappearance of Sugar. The return of sugar demands fasting for twenty-four hours or until sugar-free. The diet preceding the reappearance of sugar is then resumed except that the carbohydrate should not exceed half the former tolerance until the urine has been sugar-free for two weeks, and it should not then be increased more than 5 grams per week.

Weekly Fast Days. Whenever the tolerance is less than 20 grams carbohydrate, fasting should be practised one day in seven; when the tolerance is between 20 and 50 grams carbohydrate, 5 per cent. vegetables and one-half the usual quantity of protein and fat are allowed upon the fast day; when the tolerance is between 50 and 100 grams carbohydrate, the 10 per cent. and 15 per cent. vegetables are added as well. If the tolerance is more than 100 grams carbohydrate, upon the weekly fast day the carbohydrate should be halved.

Bread is seldom prescribed, because it is so easy for a patient to overstep the limits. Many patients use bread substitutes, such as Huntley & Palmer's Akoll Biscuits, Barker's Gluten Flour[2] (Brand A), Hepco Flour,[3] Lyster Bros'. Diabetic Flour, Whitefield, New Hampshire. The quantity of fat which it is necessary to give a severe case is considerable. A diabetic weighing 60 kilograms requires at least 30 calories per kilogram body weight to be up and about the hospital, with an occasional walk. Since in the severe cases not more than 10 grams carbohydrate, representing 40 calories, can be given in this form, and seldom more than 75 grams protein (1.25 grams per kilogram body weight) which would amount to 300 calories more, the balance of the diet must be made up of 150 grams fat, amounting to 1350 calories, and even more unless 15 grams alcohol are given, which would amount to 105 calories.

Table VII.—Quantity of Food Required by a Severe Diabetic Patient Weighing 60 Kilograms.

Food	Quantity grams.	Calories per gram.		Total calories.
Carbohydrate	10	4	=	40
Protein	75	4	=	300
Fat	150	9	=	1350
Alcohol	15	7	=	105
		Total	=	1795

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[2] Herman Barker, 433 Broadway, Somerville.

[3] Waukesha Health Products Co., Waukesha, Wisconsin.

The quantity of fat (150 grams to 160 grams) is easily given in the form of 120 c.c. of 40 per cent. cream (48 grams), 15 grams of oil (15 grams) and 3 eggs (15 grams), bacon (cooked) 30 grams (15 grams), meat, cooked, 100 grams (5 grams), and butter 60 grams (50 grams). These figures are only approximately correct.

Should the patient remain sugar-free and the weight be maintained upon this diet, gradually the quantity of fat could be lowered and the carbohydrate increased. A very few of my patients have a tolerance for between 200 and 300 grams of carbohydrate. With most, the tolerance is below 100 grams, and with the majority it is under 50 grams.

The patient should have one day of restricted diet each week, no matter how mild the case. This is done partly to spare the function which controls the carbohydrate metabolism, but also to remind the patient of what a strict diet really is. The patient is told to gain little or no weight, and as Dr. Allen advises, not to come up to his former weight. The severer cases examine the urine daily, and the milder ones once a week. The patients are instructed to lead less strenuous lives. Unfortunately, they feel so well that often this advice is disregarded, and I believe that all of us err in allowing our patients to do too much. They should have nine hours in bed at night, and should have a quiet hour of rest each day, no matter how well they feel.

Patients must be followed up. The secret by which this is brought about lies in instructing the patient how to live in the first few days of treatment, and making him understand that he must always be under supervision. This is sometimes difficult, for a doctor does not like to force a patient to come to him. Fortunately, improvement in the treatment of diabetes is rapid enough to enable a physician to repay his patient for a visit with new ideas at comparatively short intervals.

The after treatment of diabetic patients is quite as important as the initial treatment. Patients must learn to keep sugar-free and maintain weight, and when difficulties occur report for advice. There is not the slightest doubt, in my opinion, that even under the old regime the patients who were kept under judicious supervision did better than those who neglected treatment.

Many dangers suggested themselves when I commenced to use the fasting treatment, but most of these have gradually faded away. It is still true that a patient who undertakes the treatment and then relapses to former slack methods is worse off than his untreated brother. Liability to infection is not common. A child, Case No. 813, of eight years acquired tonsillitis and developed an otitis media, but this was a circumstance not unusual for any hospital patient. In another direction an unlooked for danger has appeared. Owing to the apparently easy control of diabetes, several diabetic married women have seen no reason why they should not become pregnant. So far I have treated but one case under the new regime, and that patient did well. How other patients will do I cannot predict.

More difficulties will arise in the introduction of the newer methods of treatment from the physician than from the patient. Physicians who have only an occasional case of diabetes under their care, and in general mild ones, will not take the time or see the necessity of keeping their patients sugar-free. It is the same experience with which we are all familiar in pulmonary tuberculosis. A number of physicians who have had serious cases have become interested and investigated the treatment, and these report excellent results. In several instances fasting has been carried out most successfully by the family physician at home. The difficulty will arise in prevailing upon the physician to carry out protracted fast in the severer types of the disease. This takes real courage, and it is desirable that all who have had good results with severe cases should publish their reports. The doctor in the hospital clinic can easily handle the patient, but it takes time to educate the family and all the friends.

No one can tell how well diabetic patients will do in the future. It is surprising to me to note how much better my patients have done during the last six months, and to note that those cases which have followed most carefully the restricted diet and fasting have done the best. So far, no patient whom I have taught to do his own urine during the last year has died. I am coming to feel that coma no longer represents the culmination of the disease, but that it is an avoidable accident.

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RELATIVE PULMONARY INSUFFICIENCY (GRAHAM STEELL MURMUR).

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In 1888 Graham Steell,[1] in discussing the physical signs of mitral obstruction and regurgitation, wrote as follows: "Mitral diastolic murmurs of less intensity are, however, not infrequently heard best to the left of the sternum just below the pulmonic area about the sternal end of the fourth rib and downwards for a little way over the right ventricle. Again, a still finer, in fact a soft blowing diastolic murmur, is not very rarely to be heard in the pulmonic area itself as well as for a short distance below it. There can be no question of the occurrence of such a murmur in a few cases of mitral stenosis, but its interpretation has been a matter of dispute. It is difficult to accept the view that it is a direct mitral murmur owing to the softness, and it has been suggested that it is really a murmur of coexisting aortic regurgitation. The diastolic murmur of aortic regurgitation may undoubtedly be propagated into this region, as if by predilection, when it is feeble; but in the cases of mitral stenosis in which I have observed this murmur there was no evidence of aortic regurgitation in the pulse or otherwise. I have thought that the murmur in question may be explained by a trifling leakage taking place through the valves of the overdistended pulmonary artery, just as we know that regurgitation occurs under similar conditions in the case of the aorta. I once observed a case of cirrhosis of the lung which I interpreted in this way."

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[1] Med. Chron., 1888, viii, 89.

In 1906 he wrote[2] as follows: "The diastolic murmur in the pulmonic artery may, as already noted, accompany congenital stenosis, being due to the coincident deformity and incompetence of the valves. Such a murmur is not a rare occurrence in cases of long-standing mitral stenosis. When first established it usually comes and goes according to the degree of blood-pressure within the vessel. It is accompanied by dilatation of the pulmonic artery, which, as already stated, under the circumstances may become atheromatous like the aorta. This murmur has been called the murmur of high pressure in the pulmonic artery."

It would appear from this that Steell had frequently heard this murmur, but in an article published between the appearance of his first article on the subject of mitral stenosis and his text-book upon *Diseases of the Heart,* he gave a statistical analysis of fifty cases of mitral stenosis. Discussing the diastolic murmurs heard in these cases, he states that in Case 46 there is some ground for belief that the murmur representing the murmur of high pressure in the pulmonic area which he had described was present. It appears, therefore, that this murmur was doubtfully present in not more than 2 per cent. of his cases, and probably, had his observations been extended, in a considerably smaller percentage. Although he speaks of the fact that the occurrence of this murmur is associated with dilatation of the pulmonic artery, he brings forward no definite proof that such a dilatation occurs, for it does not appear in any case that he found such a dilatation postmortem. At least no such finding is mentioned, and it seems reasonable to conclude that it would have been.

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[2] Diseases of the Heart, Manchester, 1906, p. 105.

This murmur has attracted little, if any, attention from other clinicians. It is not mentioned by McKenzie nor by Hirschfelder, nor have I, to the best of my recollection, come across reference to it in literature excepting in the articles by Steell himself. Nevertheless, it seemed to me not unreasonable that such a murmur should occur, and in all cases in which there was reason to suspect high pressure in the pulmonary system I have attempted to discover its existence. I believe that I have been able to identify it in three cases. It is heard as a soft, blowing systolic murmur, smooth, usually rather distinct in character from other murmurs in the heart, heard most distinctly just beneath the pulmonic cartilage, and transmitted obliquely downward and to the right to a point just below the junction of the third costal cartilage and the right border of the sternum. It commences with the second sound and terminates before the first. In none of these three cases in which I think I heard it was it loud. There was no accompanying thrill. The second sound was distinctly audible, but not accentuated. Of these three cases, one died and permission was refused for autopsy, one passed from observation, and the third is the case I wish to report.

W. M., male, white, aged seventy-eight years, was admitted to the Philadelphia Hospital, January 21, 1907, complaining of dyspnea and loss of appetite. He apparently improved and was transferred to the out-wards, where he remained until, on account of increasing disability, he was transferred to my service on the medical floor the latter part of October, 1914.

The family history was negative. He did not recall any of the diseases of childhood. He had had rheumatic fever about twenty years ago, but otherwise had been in good health until his admission to the hospital. He denied syphilis or gonorrhea. At times he drank heavily, chiefly whisky. He did not recall any injuries or surgical operations. For the past three years he had noticed that his wind was poor. There was constant slight dyspnea, increased by any exertion. He had a chronic cough and expectoration, but the sputum was not bloody. Sometimes he suffered from constipation. For three days before his admission to the medical ward he had been vomiting greenish material. This was the first sign of gastric disorder.

The notes of the physical examination are as follows: A well-nourished adult white male; contracted but normally reacting pupils; poor teeth; apex beat in the sixth interspace one-quarter of an inch to the left of the mammary line. The first sound at the apex was distinctly loud. The second pulmonic sound was quite distinct. There was a diastolic murmur heard at the junction of the left third costal cartilage of the sternum which could be traced downward and to the right for a short distance. It was of a soft, blowing character and terminated before the first sound. The second aortic was distinctly accentuated. The heart's action was irregular. The pulse was small and irregular. The artery was palpable. There was no indication of a Corrigan pulse. There was evidence of consolidation at the apex of the left lung and some rales at the base of both lungs. The liver and spleen were not enlarged. There were no areas of tenderness in any part of the abdomen and no abnormal masses. The fingers were moderately clubbed. There were brown pigmented areas in the tibial regions of both legs.

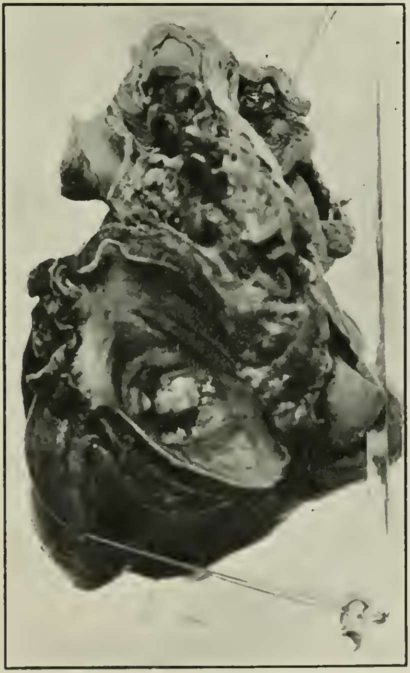

Fig. 1.—View of mitral valve through the left auricle, showing the extreme stenosis.

A diagnosis was made of hypertrophy of the heart; arteriosclerosis; mitral disease and possibly Graham Steell murmur. In addition, tuberculosis of the left apex was noted as probably present, and it was supposed that there was an old pleuritis of the right base. A Roentgen-ray examination was made and reported a dilated aorta.

The patient grew steadily worse. On October 17 there was Cheyne-Stokes breathing and the vomiting continued. On October 18, a loud presystolic rumble was heard at the apex, and a loud systolic murmur, which was transmitted to the left but not into the vessels of the neck. The arrhythmia had become very pronounced. On November 3, Cheyne-Stokes breathing had returned and the patient was very weak. The pulse was feeble and arrhythmical. The presystolic rumble had disappeared. Both lungs were full of rales. On November 7 the patient died. The urine was negative. There was no blood count and no Wassermann reaction. A second Roentgen-ray, made particularly with reference to the lungs, reported that they were apparently normal, that there was considerable dilatation of the aorta, and that the heart was moderately hypertrophied, particularly on the right side.

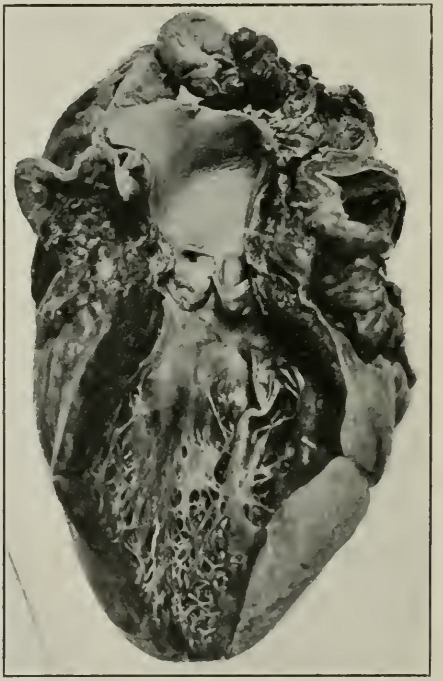

FIG. 2.—View of cavity of the left ventricle, the aortic valve, and the first portion of the aorta. All pictures made with lens at same distance from the heart.

An autopsy was made the following day and the notes are exceedingly minute, and are interesting partly because of the things not observed, partly because of the things found that were not suspected. Of the latter the most important was cholelithiasis, ulcerated cholangeitis, acute fibrous pericholecystitis, and cholangeitis. In spite of the Roentgen-ray, tuberculosis was found at the apex of the left lung, and numerous adhesions were found at the base of the right pleura. A small amount of fluid was found in the pleural cavities. The notes on the heart may be given in full. They are as follows: "The heart shows the left ventricle dilated, with some thickening of the wall. Musculature fairly firm, cloudy appearance. Endocardium grayish. Aortic leaflets thickened along the base. Papillary muscles show fibrous tips. Pulmonary leaflets show congenital fenestrum. Coronary arteries show several elevated thickenings along course." . . . "Spreads made from curtained material in gall-bladder show encapsulated diplococci, probably pneumococci and an unidentified bacillus."

The specimen was preserved at my request, and upon examination the following notes were made: The wall of the left auricle is greatly thickened. There is a buttonhole mitral valve, the orifice of which is irregular, its greatest diameter being less than five millimeters. The wall of the left ventricle is only moderately hypertrophied. The aortic leaflets are slightly thickened. The aortic orifice is 4.6 cm. in circumference. The wall of the right ventricle is slightly thickened. The circumference of the pulmonary orifice is 7.8 cm. The circumference of the pulmonary artery, 2 cm. above the orifice, is 7.8 cm., and of the aortic artery, 2 cm. above the orifice, is 4.7 cm. The pathologist's notes may therefore be amended to read "hypertrophy and dilatation of the left auricle;

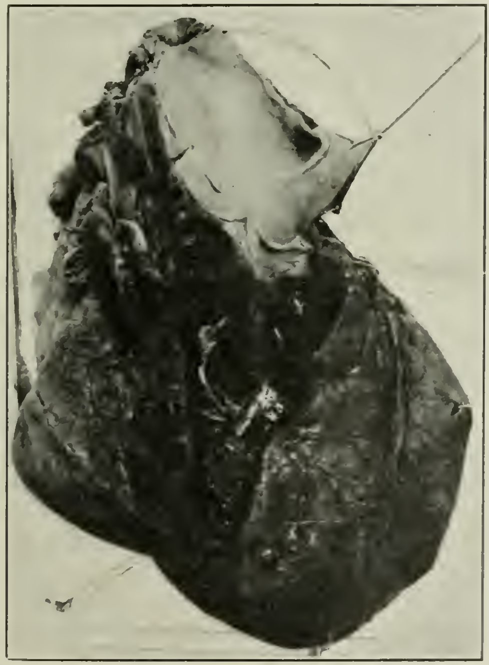

Fig. 3.—Partial view of the cavity of the right ventricle of the pulmonary valves and the first portion of the pulmonary artery.

extreme mitral stenosis; dilatation of the pulmonary artery and moderate dilatation and hypertrophy of the right ventricle."

It is, I think, of some interest that the Roentgen-ray examination was at fault in two particulars: the dilatation was of the pulmonary artery and not of the aortic, and the lungs were not normal. The pathologist is apparently at fault in overlooking the mitral stenosis and the dilatation of the pulmonic artery. As the mitral stenosis was not recorded either in the autopsy notes or in the pathologist's diagnosis, it is fair to assume that the mitral valve was not particularly examined. If the heart had not been preserved it would of necessity have been assumed that mitral disease did not exist, and that therefore the clinical observation of a Graham Steell murmur was inaccurate. At the subsequent examination, however, the existence of mitral stenosis and of dilatation of the pulmonary artery in conjunction with the physical signs observed during the patient's life accord with the conditions postulated by Graham Steell as necessary for the occurrence of the murmur, and it seems reasonable to conclude that a functional insufficiency of the pulmonary valve secondary to the mitral stenosis was present in this case.

The value of the discovery of the Graham Steell murmur is not at the present time evident. Unquestionably in those cases in which pressure on the pulmonary circulation is so increased that the artery is dilated and the pulmonary valves thereby become incompetent the prognosis is not so favorable, but it does not appear in these cases that restoration of compensation is therefore impossible. It may be that with the accumulation of observations more definite significance can be attached to it. It does indicate, however, quite definitely and positively in all the cases in which I have seen it, the existence of decompensation, and hitherto always of a severe type.

THE SOY BEAN AND CONDENSED MILK IN INFANT FEEDING.

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In 1909 I called attention to the soy bean,[1] and suggested its use in infant feeding. Two years later, having become convinced of its value, I submitted a report, with a short article,[2] before the American Pediatric Society. In the meantime, in order to bring the subject before the medical profession, another article was published.[3] In addition to its use in infant feeding the bean has been used in diabetes, and Friedenwald and myself called attention to the work which had been done on this subject, and published[4] an account of our own experience in this regard. This article brought so many requests for information about the preparation of the bean, that a short article on its cooking followed.[5]

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[1] The Soy Bean in Infant Feeding, Preliminary Report, Arch. Pediat., July, 1909.
[2] Further Observations on the Soy Bean, Ibid., October, 1911.

Inasmuch as the bean is still practically unknown in this country, it may not be out of place to review briefly the facts in connection with it. The soy bean (Glycine hispida), sometimes incorrectly called the soja bean, is an annual leguminous plant, which originally grew in a wild state from Cochin China to the south of Japan and to Java. It has been cultivated since the very earliest times in Japan, and in China long before the time of Confucius. The bean gradually found its way into India, but has been very slow in spreading to other lands. Something over one hundred years ago it was brought to Europe and grown in botanical gardens chiefly as a curiosity. It was described by numerous writers, among the very early contributions being one by Koempfer, who observed it in his travels throughout the East, and wrote about it in 1712 under the name of Daidsu. Linnaeus described it under the name of Dolicha soja, and since then many others have written about it, notably Montigny, one of the French consuls in China in 1854, and following his suggestion, in 1855, there was an attempt made to introduce it into France under the auspices of the Société d'acclimatation. It was introduced into England about 1790, but there do not seem to have been any studies made upon it from the economic standpoint. In 1875 Haberlandt started a series of investigations in Austria-Hungary, and became an enthusiastic advocate of it, publishing a book about its use as food for both man and animals. As early as 1829 Thomas Nuttall wrote an article concerning the bean as a valuable crop for the United States. When the Perry expedition returned from Japan, in 1853, the beans were again brought to this country, but up until the last fifteen or twenty years the plant seems to have been known only as a curiosity. Recently, however, studies have been made in the various agricultural experiment stations, most notably those of Kansas and Massachusetts, and since 1898 the Office of Seed and Plant Introduction of the United States Department of Agriculture has taken up the work of distributing the bean. In this country it has been grown chiefly as a forage crop, and very little attention has been paid to its use as food for man.

Like many other leguminous plants it absorbs nitrogen from the atmosphere, and is frequently used for enriching the soil, the entire plant being plowed under after it is grown upon more or less barren land. The plant itself is an erect annual, with branching stems covered with short hairs. The leaves are trifoliate and more or less hairy, and the flowers are violet or pale lilac in color. The pods contain from two to five seeds, and the different varieties of the bean vary in size, shape, color, and in the length of time they take to mature. Some are whitish, some yellow, some greenish-yellow, some brown, and some black. In shape some are spherical and some are more or less compressed. The plant varies from two to four feet in height, and bears a remarkable number of beans. The flowers are self-pollinated, which makes the yield independent of insects. Ordinarily the plant grows best in the same temperature as corn, but the different varieties differ in the length of time they take to mature, and the more rapid varieties may be grown in the North. Seven different varieties are handled by seedsmen, and some twenty-two distinct varieties are known, while in China and Japan almost every village is said to have its own strain of soy beans. The bean should be harvested early, as the pods open spontaneously, and if allowed to stay on the plants, scatter the beans on the ground. The ordinary variety ripens in from seventy-five to ninety days. A full account of the plant will be found in the *Farmers' Bulletin*, No. 58, of the United States Department of Agriculture, and of the different varieties in the *Bureau of Plant Industry*, Bulletin No. 98.

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[3] The Soy Bean as an Article of Diet for Infants, Jour. Amer. Med. Assoc., 1910, liv, 1664.

[4] The Use of the Soy Bean as a Food in Diabetes, AMER. JOUR. MED. SCI., 1910, cxl, 793.

[5] Soy Bean Cookery, Med. Rec., September 23, 1911.

The bean has been put to many uses. It is grown for silage and as a hay crop, and is used to improve the quality of the soil. The bean has been used as food for animals, especially cows and pigs. Some varieties contain large quantities of oil, which is used as a food and for illuminating purposes, as a lubricant, and also for the manufacture of paint and soap. The residue left after the oil has been expressed may be used as a fertilizer and also as food for animals.

The beans are eaten as a vegetable, in soups, sometimes picked green, boiled, and served cold with a sprinkling of soy sauce, and sometimes served as a salad. The bean forms the basis of the so-called soy sauces used as condiments all over the world. In the East it is most frequently used in the form of more or less cheese-like foods that are prepared from it. Of these there are a great variety, the best known being natto, tofu, miso, yuba, and shoyu. Natto is a sort of bean cheese made by boiling the beans until they become very soft, and then placing the resulting mass in a warm cellar, where it ferments. Tofu is prepared by soaking the beans for about twelve hours in water, and then crushing them between mill stones. They are then boiled in about three times their bulk of water and filtered. The filtrate is a white, opaque, milky liquid with a taste similar to malt. In the making of tofu the protein is precipitated by adding the mother liquid obtained by the manufacture of salt from sea water, the precipitate being made into cakes. The chemical analysis of the filtrate is as follows:

	Per cent.
Water	92.53
Protein	2.02
Fat	2.13
Fiber	0.03
Ash	0.41
Nitrogen-free extract, including carbohydrate	1.88

The large amount of nitrogen which these beans contain probably account for the small amount of meat and other animal food taken by the Japanese. According to the dietary studies made in Japan the nitrogen from the beans, especially if taken in a mixed dietary, is easily absorbed.

The soy beans are sometimes roasted and then used as a substitute for coffee. They are also sometimes served as a vegetable, first soaking the beans until the skins come off, and then boiling them until soft and serving hot. The North Carolina Experiment Station recommends the bean as a palatable vegetable, and suggests that the bean be soaked until the skins come off and they be stirred until the skins rise to the surface, when it is easy to remove them. The beans are then boiled with bacon until soft, seasoned with pepper, salt, and butter, and served hot. If the beans are green the preliminary soaking may be omitted.

In my first experiments I used the beans, but for purposes of making gruel for infant feeding they require a considerable amount of cooking, so at my request Mr. Deming, of the Cereo Company, of Tappan, New York, made a flour which is entirely satisfactory for practical use. An analysis of this flour yielded the following results:

	Per cent.
Protein N. X. 6.25	44.64
Fat	19.43
Mineral matter	4.20
Moisture	5.26
Crude fiber	2.35
Cane sugar	9.34
Non-nitrogenous extract	14.78
Starch	None
Reducing sugars	None
Polarization normal weight due to optically active substance other than cane sugar included in proteins and non-nitrogenous extract	7.86°

The percentage of protein in this flour is almost one-third greater than the percentage of protein in the whole beans. This is caused by removing the coarse, fibrous hulls which contain little protein.

Each ounce contains 13 grams protein and 120 calories.

	Protean, per cent.	Fat, per cent.	Sugar, per cent.	Calories.
¼ ounce, 1 level tablespoonful to quart	0.35	0.15	0.08	30
½ ounce, 2 level tablespoonfuls to quart	0.70	0.30	0.15	60
¾ ounce, 3 level tablespoonfuls to quart	1.00	0.45	0.23	90
1 ounce to quart	1.40	0.60	0.30	120
2 ounces to quart	2.80	1.20	0.60	240

Condensed milk as a food for infants has, of course, been well known for many years. In most instances it has been used only as a temporary expedient, either when pure milk cannot be obtained, or in traveling, or for infants who have been improperly fed on mixtures containing too much fat and protein. Condensed milk has the following compositions:

Condensed milk (Eagle Brand):

	Per cent.
Fat	9.82
Milk sugar	12.49
Protein	8.80
Ash	1.90
Cane sugar	40.50
Water	26.49

This furnishes about 102 calories per ounce, and in dilutions with water, as ordinarily used, it contains the following percentages:

	1 in 6, rarely used.	1 in 8.	1 in 12.	1 in 16.
Fat	1.66	1.25	0.83	0.62
Protein	1.50	1.12	0.75	0.56
Sugar	8.83	6.63	4.41	3.31
Calories per ounce approximate	17.00	12.8	8.50	6.40

After a considerable amount of clinical experience I found that the best method to begin feeding mixtures of soy bean and condensed milk is to make a gruel composed of one level tablespoonful of soy flour, two level tablespoonfuls of barley flour, a pinch of salt, and one quart of water. This should be boiled for twenty minutes, or even longer, and the water lost in the cooking should be replaced. To this is added condensed milk, varying from 1 to 16 to 1 to 8, according to the age of the child and other circumstances. As a rule this will be found to agree admirably, and may be used in quantities varying from 2 to 8 ounces at a feeding. The feeding interval may be two, two and a half, or three hours, usually three hours, and occasionally, in difficult cases, this may be lengthened to three and a half or even four hours; but I have not found this advisable in many cases. The amounts of condensed milk and the strength of the gruel may be varied according to circumstances, using weaker mixtures if there is vomiting, or if there are symptoms of indigestion, or if the stools, after a number of days, do not appear to be more or less normal. The stools of babies fed with soy bean mixtures are slightly brownish in color, should be perfectly well digested and smooth, not unlike in appearance those of babies that have been fed upon malted milk. In children who are not gaining, and yet who seem to be taking the gruel well, the amount of condensed milk may be increased to 1 to 8, that is, 1 ounce of condensed milk, with enough gruel to make 8 ounces, and in exceptional cases, even to 1 to 6, though I have rarely found this either advisable or necessary. The gruels may vary in composition, and in older children they may be increased to double the strength advised above, that is, 2 level tablespoonfuls of soy flour and 4 of barley, and occasionally this may be increased still further. If the soy bean is used too strong, or if it is used without a sufficient amount of carbohydrate with it, as in perfectly plain gruels without either cereal flours or condensed milk, it is liable to cause thin, dark-colored, foul-smelling stools, owing to the high protein and fat content, and the very small amount of carbohydrate present.

These mixtures of condensed milk and soy bean gruels will be found one of the most valuable additions to the dietary of the infant. On two occasions I have encountered a curious idiosyncrasy for barley flour in these mixtures. Following administration of the gruel made with barley flour, there was a sudden and marked general edema, lasting several days. It so happened that I had seen this condition from barley gruel used alone, so that this was stopped in both instances, and the gruel subsequently made with wheat flour in place of the barley flour. In both instances a second attempt to replace the wheat flour with barley was followed by the same edema, so that there can be little question as to the cause of it. As in feeding any cooked food to infants, some antiscorbutic food should be given, and for this purpose orange juice in quantities from a teaspoonful to two tablespoonfuls may be used daily, or at intervals or several days, or even once a week. I have never seen a case of scurvy resulting from these mixtures, but in all cases in which the gruel was used over long periods of time, some antiscorbutic food has been added.

The class of cases and circumstances in which this mixture is to be advised may be outlined as follows: When fresh milk cannot be obtained, or when the milk supply is very questionable; in summer, when there is some question concerning the milk supply and then in instances where the infant is found to be incapable of digesting cow's milk. It will also be found useful in certain cases of intestinal indigestion in infants who, under ordinary circumstances, can digest cow's milk, but who have had their intestinal functions temporarily deranged. It may also be of service in cases of chronic vomiting, and particularly useful as a food after summer diarrhea. Without the condensed milk the gruel may be used as a food in many diarrheal conditions with considerable advantage, but as is the case with every other food, there are many instances in which it will not agree with the child. The use of soy bean gruels alone without barley or some other cereal may be recommended under very exceptional circumstances. The failure to obtain proper results from the use of the soy bean has been largely due to an attempt to use it without the addition of some cereal. In the past six years I have had a sufficient amount of experience with this method of feeding to know that it can be used without any danger. It will not produce rickets, and with a very small amount of some antiscorbutic food, will not produce scurvy, It permits a perfectly normal development as far as bones are concerned, and in successful feeding the infants present the appearance of breast-fed babies. In some of the most difficult cases children are slow to reach the normal appearance, but most of such children that I have had have been cases which I do not believe could have been raised by any other means or only by using a wet nurse.

In order that this may be made more plain a few brief clinical histories will be given.

Case I.—W. L. C., born June 17, 1910. Weighed eight pounds at birth. Was nursed five weeks and then weaned, owing to the failure of the mother's milk. Since that time has been fed on various mixtures of milk, using Walker-Gordon milk and various diluents. It was subsequently put upon various proprietary foods, and also upon 1 to 8 condensed milk mixtures. It was first seen October 9, 1910. The weight at this time was nearly ten pounds. The baby slept well at night, and the stools were normal, rather scanty. It was exceedingly irritable during the day, and it vomited most of its food. The mother stated that the vomiting was about the same on everything that had been tried. Various milk mixtures were tried in rather rapid succession for the next month, with no result, and the weight varied between nine and ten pounds. The baby at times would be more comfortable, but was decidedly doing badly. Patient was put upon the standard gruel suggested above, with condensed milk. Gain in weight began almost immediately, and on December 4 its weight was 11 pounds 4 ounces, and the baby was returned to a milk mixture, on which it did fairly well, and by January 20, 1911, reached a weight of 14 pounds 4 ounces. At this time the food was very badly borne, and in the next two weeks the weight had dropped to 13 pounds 15 ounces, and the vomiting was again very troublesome. It was again put upon the condensed milk and soy bean mixture, and this time was kept upon this until October. The child gained steadily, and on May 25 weighed 20 pounds. This child had rather an uneventful history subsequently, except that until about a year ago was not able to digest cow's milk even if diluted. Since that time it has lost this peculiarity, and is able to digest cow's milk, although it is only with difficulty that it can be induced to take it.

Case. II.—O. S., one of the best examples of the value of this form of feeding that I have seen. Born April 21, 1914. Second child, first having died at birth; weight, 8 pounds. Was seen April 27, when it had dropped to 7 pounds 4 ounces, was crying continuously, had loose, greenish stools, appeared to have some severe toxemia, slightly jaundiced. The baby continued to nurse, but seemed extremely ill, vomited a great deal, abdomen was extended with gas to an extent that I have rarely ever seen, and there seemed to be considerable difficulty in getting relief from this condition.

Various means were tried, including bismuth and chalk mixtures, betanaphthol bismuth, lactic acid bacillus tablets, and aromatics. The child cried day and night, was unable to pass the gas either by mouth or by bowel, had numerous small greenish stools some days, and at other times was very constipated, when bowels only moved with difficulty. Owing to the worry and care of the child the mother's milk failed, and the child was first put on condensed milk, subsequently upon various modifications of milk from the Walker-Gordon laboratory. These mixtures were started at 2.5 fat, 6 sugar, 0.75 whey protein, 0.25 casein, 5 per cent. lime water and water to make 20 ounces for the twenty-four hours. The feeding time was varied from two hours to three and three and a half, but the condition remained unchanged. During the next month the usual variations were made. Changes in the percentages of fat, sugar, and protein were all unavailing. The child remained practically stationary in weight, sometimes losing a couple of ounces, sometimes gaining a couple of ounces. A second trial was made with the bulgara tablets, and subsequently milk modified with sodium citrate was tried. On July 1 the child had a remarkable attack of edema, lasting four days. This came on suddenly and was very marked, presenting the appearance of a bad case of acute nephritis; but the urine was normal, and the general condition of the child did not seem to be much disturbed. The child was then tried on half mother's milk, obtained from a wet-nurse, and half modified milk, and on July 12 a wet-nurse was obtained. Her milk was normal and the baby took it readily, but the condition remained unchanged. Owing to difficulties with the wet-nurse, this had to be discontinued. The child was taken to the country, where it came under the care of another physician. The first part of this period it was put to a wet-nurse again, but without success.

On July 21 it was put on Loeflund's Malt Soup Extract, 1 tablespoonful, flour 2 tablespoonfuls, milk 6 ounces, and water 18 ounces. Eight bottles, 2 ounces each, were fed every two and a half hours. This was increased to 2½ ounces on July 22 and 3 ounces on July 23. Stools were well digested, but there was considerable difficulty with gas. The Malt Soup Extract was increased slightly, and on July 24, the baby had a severe diarrhea—twelve stools a day. This continued until July 27, when there was still considerable mucus and some blood in the stools. Baby was given Mellin's Food, one ounce in 8 ounces of water, 3 ounces every three hours, to alternate with three breast feedings.

July 30. Mellin's Food, 1 ounce, milk 4 ounces, and water 7 ounces. Four ounces were given at a feeding. The weight during all this period was approximately 7 pounds 9 ounces. Some days it gained an ounce or two, some days it lost an ounce or two.

On August 7 it was given peptonized milk 6 ounces, Mellin's Food 1 ounce, and water 14 ounces; four bottles of 4 ounces each, and 3 breast feedings. On this it increased on August 10 to 7 pounds 12 ounces, and on August 12 to 8 pounds 1 ounce. It was then given Mellin's Food 2 tablespoonsful, cream ½ ounce, peptonized milk 8 ounces, water 12 ounces; 4 ounces at a feeding, subsequently increased to 4½. On this mixture the baby was distinctly better, the abdominal distention improved, the stools thin, but apparently well-digested.

August 21. Weight 8 pounds 4 ounces.

August 28. Given peptonized milk, 9 ounces, water 11 ounces, Mellin's Food 3 tablespoonfuls.

August 31. Weight 8 pounds 14 ounces. Then followed an attack of indigestion. The baby was again placed on breast milk. There being no improvement on this, it was discontinued.

September 7. Mellin's Food 1½ ounces, milk 6 ounces, water 14 ounces; 4½ ounces at feeding, 7 bottles. Weight 8 pounds 7 ounces.

September 10. Mellin's Food 3 tablespoonfuls, milk 8 ounces, water to make 35 ounces. There was marked abdominal distention, and the stools varied, some being well digested, others containing curds, and being greenish in color. From this time up until October 23, patient was given various mixtures, sometimes malted soup, sometimes peptonized milk, and various formulæ.

The baby returned to town, and again came under my care on October 23. At this time it was taking a mixture of malted soup and flour and milk and water; was in almost constant pain; the abdomen was enormously distended. It was placed on standard soy bean gruel, using wheat flour in place of barley, and condensed milk 1 to 8, 4½ ounces to a feeding, The weights on this gruel were as follows:

November 10. Weight 10 pounds.

November 17. Weight 10½ pounds.

December 3. Weight 10 pounds 13 ounces; feedings increased to 5 ounces.

December 8. Weight 11 pounds 9 ounces.

December 15. Weight 11 pounds 13 ounces; feedings increased to 6 ounces. Stools on this mixture have been normal; baby still has a great deal of gas, but is much more comfortable. Had one severe attack of bronchitis.

December 23. Weight 11 pounds 15 ounces.

December 27. The baby was greatly disturbed from some unknown cause, acute diarrhea.

December 29. Weight 11 pounds 12 ounces; diarrhea stopped.

January 4, 1915. The baby was coughing a great deal, with a great deal of wheezing.

January 6. Weight 12 pounds 7 ounces.

January 13. Weight 12 pounds 13 ounces.

January 20. Weight 13 pounds 7 ounces.

January 27. Weight 14 pounds 2 ounces

February 3. Weight 14 pounds 5 ounces.
February 10. Weight 14 pounds 10 ounces.
February 17. Weight 15 pounds 2 ounces.
March 25. Weight 17 pounds 9 ounces.

Only a few of the difficulties of this case are noted above, but the account gives a fair idea of what was encountered, omitting numerous incidents which did not have any effect upon the child's development.

CASE III.—W. J. S., born September 28, 1913; first child, normal labor. Weighed at birth 6½ pounds. First seen on May 23, 1914. This baby was nursed for four weeks, was then put on modified milk, using a large number of different formulæ, none of which agreed with the child. The baby gained a few ounces from time to time, but remained very thin, and presented a typical marantic appearance, vomited almost continuously, and cried all the time. Following the use of modified milk was a period in which condensed milk, malted milk, and various modifications with Mellin's Food, were used. In February the child was removed to an infant hospital, and eventually placed on breast milk, and after three months of this treatment the baby was returned home, having gained up to eleven pounds. While in the hospital he was changed to a mixture of milk and water, and was given three level tablespoonfuls of cooked farina three times a day. During the month prior to my seeing the baby he had gained two ounces. The child was exceedingly uncomfortable. Nothing abnormal was noted in the physical examination beyond what was stated above. An effort was made to increase the milk, and an addition was made of barley water to it; but this was not very successful, although the baby gained five ounces on it, it continued to be very uncomfortable and to vomit.

On June 1 the baby was changed to a mixture of soy bean and barley, one level tablespoonful of the former, and two of the latter to one quart of water. To this was added condensed milk 6 drams, with sufficient gruel to make six ounces. Six feedings of this were given at three-hour intervals. By June 13 the baby weighed 11 pounds 9 ounces; by July 6, 12 pounds 2 ounces.

On August 1 it weighed 15 pounds and became upset from overfeeding. During this period I was out of the city.

On September 14 it weighed 14 pounds 5 ounces, and at this time he had been on a mixture of cow's milk and oatmeal water.

On September 26 milk and egg were added every other day to the food, and subsequently the gain in weight was rather uneventful.

On October 31 it weighed 16 pounds 3 ounces, and on February 15, 1915, it weighed 22 pounds. During this time he had been on a mixture of 40 ounces of milk, 2 ounces of lime water, and 8 ounces of diluent, part of the time barley water, part of the time oatmeal water, and part of the time plain water. In addition to this he was given farina and other cereals, with the addition of the soy bean flour cooked with the cereal. The appearance of the child is now practically normal.

Case IV.—L. C. F., born January 1, 1913; first child, normal labor. Weighed 8 pounds 12 ounces at birth, and gained steadily until March 30, when it weighed 11 pounds 2 ounces, and continued to lose weight until April 5, when it weighed 10 pounds 15 ounces. The mother's milk was found to be low in fat and rather scanty, and the usual means of improving the milk were unavailing. The child was weaned and placed upon a mixture of milk, barley water, and milk sugar, which agreed very well, but on which the child did not gain in weight.

On May 2 the child was given standard mixture noted above of soy bean, barley water, and condensed milk, and from this time on the baby averaged about 4 ounces a week gain, and a perfectly uneventful year following, presented the appearance of a breast-fed baby. During this year the place of residence was frequently changed, and the baby was kept upon the mixture to prevent the child getting spoiled milk, in many of the places there being no adequate milk supply.

Case V.—J. M., born July 11, 1913. Child weighed 6 pounds 14 ounces at birth, was nursed up to about October 25. Highest weight reached was 8 pounds 12 ounces about the end of September. It was first seen November 13, 1913, when it weighed 8 pounds 7 ounces. It was on a mixture of milk and oatmeal water. Was vomiting some and gradually losing weight. Was placed upon the standard soy bean and barley gruel, started on 2 drams condensed milk, with sufficient gruel to make 4 ounces, and fed at three-hour intervals. It was gradually increased up to 1 to 8.

On November 17 the baby weighed 8 pounds 12 ounces, and presented a perfectly normal and comfortable appearance.

On December 13 weight 11 pounds, and from this time the patient had a perfectly uneventful year. At the end of the first year it weighed 22 pounds, perfectly normal in every way, and had no digestive disturbances.

A STUDY OF SPLENIC ENLARGEMENT IN EARLY SYPHILIS.

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When one considers the uniformity with which the entire lymphatic system is attacked early in the course of acquired syphilis, it might naturally be expected that the spleen as well as the other lymphatic structures would take part in this general hyperplasia. It is a surprising fact, however, that an exceedingly scant literature exists which has to do with hypertrophy of the spleen in the early stages of the infection. The numerous texts on syphilology make but brief mention of the fact, and all seem agreed that it is only occasionally that one finds enlargement of the spleen in acute syphilis.

From the results of our studies, it seems beyond a peradventure of a doubt that these brief and cursory references in the literature on enlargement of the spleen in early syphilis are not due to its non-occurrence, but rather to the fact that the subject has received from clinicians but very little study. This is probably due to the fact that syphilis is, and has been for the most part, an ambulatory disease. Hospitalization of the syphilitic is observed only in a few institutions, and a careful study of the visceropathies incident to secondary syphilis are, for this reason, not always possible.

The first reported case of splenic enlargement in association with secondary syphilis was published in 1862 by Biermer.[1] This author noted in a woman, aged twenty-eight years, eight months postinfectionem, marked enlargement of the liver and spleen, together with a roseola. Under treatment the spleen rapidly decreased in size, the liver, however, remaining enlarged.

The credit for first calling attention to the acute splenic hypertrophy in secondary syphilis belongs to A. Weil.[2] This author, in 1874, published observations on three cases of secondary syphilis in which he was able to percuss enlargement of two and palpate a definite tumor in the third. Mention must also be made of the observations of Gold,[3] who, in 1880, published the report of a postmortem on a case of secondary syphilis in which slight enlargement of the spleen was noted. Inasmuch as this patient also had an erysipelas, it may be questioned whether the splenic enlargement was due to this cause rather than to the syphilis.

In 1895 Columbini[4] stated on the basis of his investigation that enlargement of the spleen was a uniform finding in all cases of fresh syphilis, coincident with the appearance of the exanthem. Discussing Columbini's results, Bruhns[5] in 1899, called attention to the fact that the former's results were largely the result of percussion of the enlarged organs, at the same time pointing out the great difficulties in determining splenic enlargement in this way.

This last author investigated 60 cases of recent syphilis, and was able to reëxamine them frequently during the entire first months of treatment. In addition to these sixty cases of early syphilis he examined four of precocious malignant syphilis. The spleens were examined twice weekly and percussion of the organ was always supplemented by palpation. It is surprising to note that of these 60 early cases, Bruhns was able to demonstrate definite enlargement in only 4. In the precocious malignant cases 2 out of the 4 were found to have enlarged spleens. Bruhns found, therefore, 10 per cent. of his early cases with definite palpable tumors, and in not one of these was there any other possible explanation for the enlargement considered present. In 5 out of the 6 cases the enlarged spleen rapidly disappeared under the influence of mercurial therapy.

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[1] Schweizerische Ztschr. f. Heilk., 1862, i, 118.

[2] Deutsch. Arch. f. klin. Med., 1874, xiii, 317.

[3] Vierteljahrsschrift f. Derm. u. Syph., 1880, xii, 463.

[4] Instituto dermosifilopatico della universita di Siena, 1895, cited by Bruhns.

[5] Deutsch. Arch. f. klin. Med., 1899, lxiv, 450.

The next observation of note was that of Wewer,[6] in 1876. This author found enlargement of the spleen 6 times in 79 cases of secondary syphilis. Haslund,[7] who has perhaps devoted more space than any other author, either before or since his time, to splenic syphilis in general, expressed himself as believing splenic tumor in early syphilis as a rare finding.

Nolte[8] examined 50 cases of secondary syphilis and found enlargement in only 2. The largest figures next to those of Columbini are those of Avanzini,[9] who found enlargement in 8 out of 30 cases, slightly more than 25 per cent. Schuchter,[10] in 1887, reported 6 cases out of 22 in which the spleen was enlarged; figures almost identical with those of Avanzini, who, however, found only 16 cases of enlargement of the spleen in 490 cases examined. Unfortunately, however, it is not noted how many of these 490 cases were recent infections, and Bruhns calls attention to the fact that many were probably in the latent stage and later period of the disease.

The great difference of the figures quoted is undoubtedly due to the differences in the methods of examination. It need hardly be mentioned here that percussion of the spleen in determining slight deviations from the normal in its size is wholly unsatisfactory. The figures, therefore, which are based upon this means of physical examination can hardly be reliable. Not only may the difference in the percussion note be modified by the position of the stomach or colon, but, on the other hand, splenic dulness may in some cases be impossible to elicit under the most favorable circumstances. On the other hand it is very difficult to explain the large number of spleens found by palpation alone, by us, as compared with the small number reported by some of the earlier observers.

During the past two years at the University Hospital, observations have been made under ideal conditions. At our institution syphilis is not treated in the ambulatory fashion. The average length of the time that patients remain is about eighteen days; a large part of this time is spent in bed, and careful observations on such patients are therefore made possible. We have selected for the purpose of this study 100 cases of early syphilis; of these 9 cases were primary syphilis alone, the remaining 91 were cases in the first months of the infection, for the most part with cutaneous or mucous membrane involvement.

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[6] Deutsch. Arch. f. klin. Med., 1876, xvii, 459.

[7] Haslund, Arch. f. Derm. u. Syph., 1882, xiv, 346; Hospitalstid, 1882, Nos. 2 and 3.

[8] Inaug. Dissert., Greifswald, 1883.

[9] Vierteljahrsschrift f. Derm. u. Syph., 1884, xvi, 379.

[10] Wien. med. Bl., 1887, Nos. 41 and 42, pp. 1290 and 1320.

METHODS OF STUDY. The patients were studied with particular reference to several different factors. Thus in each case there were noted the general adenopathy; blood findings; the general health; type of eruption; involvement of the bones; involvement of the nervous system; the course of the splenic tumor, if this were present.

GENERAL HEALTH. Under the heading of general health is meant the constitutional disturbances attributable to the infection; slight anemia with a loss from two to five pounds in weight; mild asthenia was rated as a slight effect on the general health. A moderate effect on the general health was regarded as including a blood picture of 3,500,000 to 4,000,000 red cells, a hemoglobin of 70 per cent., a sharp drop in weight from 5 to 15 pounds, malaise, anorexia, and in some cases bone involvement. Under severe involvement of general health are included those cases in which there was marked prostration, loss in weight from 15 to 50 pounds (syphilitic cachexia), severe central nervous disturbances, and cases with pronounced anemias.

It must also be noted that very few of our cases had received treatment prior to their entry into the hospital. In all cases careful examinations were made to exclude the possibility of other infections as possibly causing the splenic tumor. Realizing the inaccuracy of percussion, we have included in this study only those cases in which the spleen was definitely palpable.

GENERAL SUMMARY OF THE FINDINGS. Of the 100 cases examined, definite splenic enlargement was found in 36. The spleen was noted as being hard and firm in 17 cases, in 6 it was noted as tender, and in 3 as very soft.

Of the 36 positive cases the general health was definitely affected in 27 and the remaining 9 showed no impairment of the general functions. Severe involvement of the general health was found in 4 cases. This entailed in 1 case a loss of 50 pounds in weight. Expressed in terms of percentage, 78 per cent. of those cases in which the spleen was enlarged were cases in which the general health suffered considerable deterioration. On the other hand it must be noted that the general health was affected in 22 per cent. of the cases in which enlargement of the spleen was not present.

Definite involvement of bone, including under this heading ostalgia, arthralgia, periostitis, and arthritis, was found in 15 of our 36 cases, or in 41 per cent.

Central Nervous System. Of the 36 cases in which the spleen was found to be enlarged, 25 were available for the study of the spinal fluid, although all were subjected to a careful neurological examination. Of the 25 cases in which both the neurological examination and the spinal fluid was studied, 19 showed definite involvement of the nervous system. Such involvement took the form of basal meningitis; meningomyeloencephalitis; neuroretinitis; loss of bone conduction, as shown by the functional test of the cochlear and vestibular portions of the eighth nerve; sluggishness of the pupillary reactions; seventh nerve palsy. Of this last rare finding there were 2 cases in our series. Expressed in terms of percentages, therefore, in 76 per cent. of those cases in which the spleen was enlarged there was definite involvement of the nervous system.

Type of the Exanthem. Studying the figures here it is interesting to note that of the 36 positive findings, 19 occurred coincident with a papular efflorescence; 16 cases of the 36 had associated mucous membrane findings, 4 had alopecia. In 2 out of our 9 primary cases the spleen was definitely palpable; in both of these there was as yet no general adenitis, nor was there any sign of hematogenous infection.

Blood Examination. The blood examinations in this series were for the most part done by the senior students of the University of Michigan, and as each blood count was not controlled by us, we feel that too much stress should not be placed on these figures. It is interesting to note, however, that in 27 cases in which counts were made (presumably carefully), 14 showed a leukocytosis of over 10,000, and of 40 cases in which blood examinations were made and in which no splenic tumors were demonstrable, 16 had a leukocytosis of over 10,000. Expressed briefly then there was a preponderance of leukocytosis in those cases in which the spleen was enlarged.

With regard to the type of the splenic enlargement, by far the largest number were firm and readily palpable. The average enlargement extended about two finger-breadths below the costal margin. One cannot describe this type of hypertrophy any more accurately than by saying it closely resembles in consistence the spleen of chronic malaria. The softer spleens, of which there were 19 in our series, presented fully rounded margins, and were distinctly of the type that one encounters in typhoid fever and other acute infections.

We were particularly interested in noting the course of the splenic tumor under proper antisyphilitic therapy. In general, we must conclude from our study that the enlargement disappears much more slowly than do the other earlier manifestations. This observation parallels that with regard to the slow disappearance of the general adenitis. In one of our cases there was a persistence for over three months, and in a second the spleen resumed its normal size only after eight salvarsan injections were given. In one case the enlargement disappeared after a single injection of salvarsan. The largest number persisted until from three to five injections had been given and until mercury had been begun. The most interesting finding appeared in one case in which prior to the injection of salvarsan the spleen was not palpable, but became so following the first injection and became larger following the second injection of salvarsan.

The incidence of pain and tenderness on pressure were noted in 6 cases, in one at least pain was noted as exquisite. In this case, however, although the enlargement persisted for a considerable time, the pain was very promptly relieved by the antisyphilitic treatment.

We are not in a position to state definitely as to the time of the appearance of the splenic enlargement. In all but one of our cases, as has been noted, the enlargement was found on the first examination. Inasmuch as we found enlargement, however, in two cases of primary syphilis in which indeed the secondary manifestations never developed, it seems reasonable to assume that this condition may antedate the appearance of the other secondary manifestations.

The question naturally arises as to which of the types of splenic enlargement, hard or soft, develop into the later, or interstitial splenitis of late syphilis. With regard to this we noted in general that the softer spleen receded much more rapidly than did those of the firmer consistency. It seems not unlikely, therefore, that the harder persistent types are those which one might expect to develop the later interstitial splenitis, the softer tumors resembling more those of an acute infection and receding with the disappearance of the infectious agent from the blood.

Inasmuch as we based our findings solely on palpation, it must be very evident that 36 per cent. does not represent the total number of splenic enlargement in the cases examined, but simply the number in which the magnitude of the spleen had reached such size that it could be felt below the costal margin. We are inclined to believe, therefore, with Columbini and with Avanzini that the spleen is enlarged in a great majority of all cases of syphilis which go untreated during the first months of infection.

The interesting feature in connection with the persistence of the splenic enlargement lies in the possibility that this organ acts as a reservoir for the spirochetes or their "rest forms," and that the subsequent tertiary manifestations may possibly be due to reinfection of the blood stream from the spleen rather than, as is generally accepted now, that such lesions are recurrences *in loco* of early dissemination. Analogy at least is possible in the cases of malaria in which the spleen acts as the main point of redistribution of the organisms.

From the results of our studies we venture the following conclusions:

1. Acute splenic enlargement occurs in a large number of cases of early syphilis.
2. This enlargement may be present before the secondary manifestations are apparent, and probably represents the earliest syphilitic visceropathy.
3. The enlargement is either in the form of a soft tumor not unlike that of any other infection or may present itself as a firm, tense tumor.
4. In a small proportion of cases, tenderness, occasionally extreme, may be present.
5. The enlargement is most frequently found in those cases in which the general health has been seriously involved.
6. Acute splenic enlargement in early syphilis tends to disappear under treatment, but may persist and resist treatment longer than any other early manifestation.
7. A striking finding was the frequency with which the splenic enlargement was noted in association with early central nervous manifestations.
8. In no cases in our series was the spleen tumor associated with enlargement of the liver.

CHRONIC LEAD-POISONING IN GUINEA-PIGS: WITH SPECIAL REFERENCE TO NEPHRITIS, CIRRHOSIS, AND POLYSEROSITIS.*

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The experiments recorded in this paper were undertaken primarily with the object of repeating Charcot and Gombault's[7] work on experimental chronic lead nephritis in guinea-pigs. The results of our experiments along these lines are somewhat disappointing, but in the course of the experiments certain interesting changes were obtained in the livers and the serous membranes of the animals experimented upon, which seem to justify more extensive publication.

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* Short notes on this work have appeared in the Proceedings of the Society for Experimental Biology and Medicine, 1912, x, 49 52.

The experiments were performed exclusively upon guinea-pigs, 28 in all. The substance introduced was the same in all cases, carbonate of lead, and it was used in the same way in all experiments, being given by mouth with the food of the animals. As a rule, about ½ grain was given three times a week, but the amount given varied somewhat in different experiments. Since the object of the experiments was to keep the animals under the influence of lead for as long a period as possible, the administration was stopped whenever untoward symptoms developed; that is, whenever the animals began to suffer seriously in their nutrition or when they developed convulsions, which were very commonly observed. On the other hand, many of the animals were given as much lead as they would tolerate, in order to get as definite results as possible.

Since the animals frequently refused their food when lead was added to it, and as they often spilled much of it in the taking, the amount of lead received by each animal cannot be given to a certainty.

All animals eventually died as a result of the continued intoxication, although many of them, except for occasional convulsions, continued in good health and in a good state of nutrition to the last. In fact, some put on an excessive amount of fat, which occurrence in similar experiments has been commented on by other investigators, for instance, by Paviot.[18]

The blood in all cases showed the typical lead anemia. Stippled cells and nucleated erythrocytes were often plentiful in the circulation. Among the latter, megaloblasts were observed frequently. At autopsy the spleen was usually somewhat enlarged; in a few cases considerably so. The venous sinuses were distended and full of erythrophages. The splenic pulp, the marrow, and the liver contained hematogenous pigment in varying amounts. In the marrow the nucleated red cells were extremely numerous and the number of megaloblasts was sometimes very large, more especially so in the long-continued experiments.

The experiments were continued for a much longer time than in any previous series of similar experiments, 13 out of 28 animals surviving for one year or more, 8 of these for two years and more, and 3 even for three years and more. One animal lived almost four years.

THE KIDNEYS. Lead evidently affects the epithelium of the kidneys in a characteristic manner. Its action resembles that of other epithelial poisons, like uranium, chronium, etc., except that it is of a much milder character. The ill effects are almost entirely localized in the distal parts of the convoluted tubules, which have been mistaken for portions of the loops of Henle by some observers. As shown in Fig. 1, the change consists in a granular degeneration of the protoplasm and a pyknotic change in the nuclei. It terminates in necrosis of the cells affected. In few cases the necrosis was preceded by fatty degeneration. Eventually the protoplasm either disintegrates, breaking up into little fragments (Fig. 1), or the cells become detached from the wall of the uriniferous tubules *in toto*. In this latter case large epithelial casts may be found in the lower parts of the tubules (Fig. 2). In some cases these are plentiful Hyaline casts were observed only occasionally. This

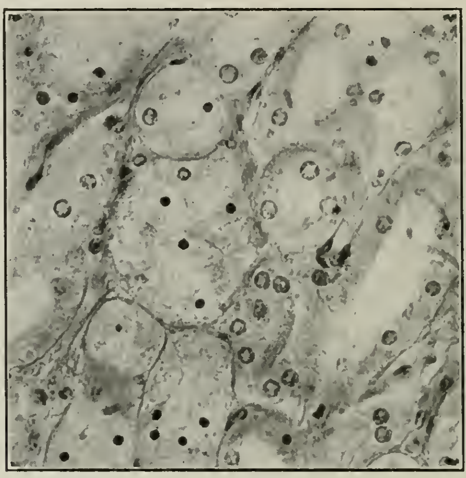

FIG. 1 (× 350).—Granular degeneration of epithelial cells in distal parts of convoluted tubules associated with pyknosis of nuclei and terminating in necrosis. Experiment 4. Guinea-pig 03.

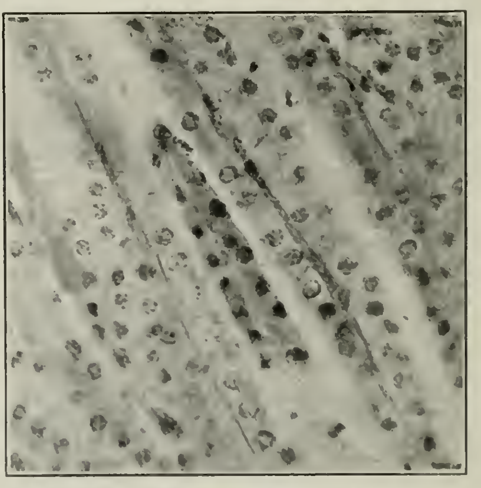

FIG. 2 (× 350).—Epithelial cast in lower part of uriniferous tubule. Experiment 18. Guinea-pig 51.

process seems to continue to practically the same extent throughout the course of the experiments, the destroyed epithelium being constantly regenerated. Mitoses may be found in fair numbers in all specimens, and in the later stages large atypical epithelial cells with giant nuclei (Fig. 3) are often encountered. Regenerated and degenerated cells are frequently seen in the same section of the same tubule. The rest of the tubules are slightly involved, if at all, except in a few cases, where the lesion is more diffuse and involves the more proximal parts of the convoluted tubules.

Examination of the urine at autopsy or during the life of the animals sometimes revealed a slight trace of albumin and commonly degenerated renal epithelium, rarely casts.

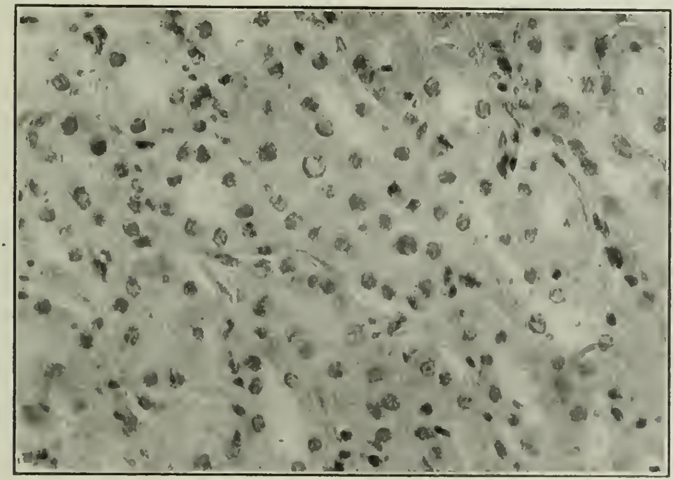

FIG. 3 (× 350).—Giant nuclei in regenerated renal epithelium. Experiment 4. Guinea-pig 03.

Characteristic red blood cells were never found in the tubules, but in some specimens shadows of them seemed to be present in some of the capsules of the glomeruli and in few tubules. In the more acute forms of experimental lead-poisoning, hemoglobinuria associated with hemorrhage seems to be the usual results; but in chronic lead-poisoning one is hardly justified in using the term hemorrhagic nephritis in the way that it is employed by Hoffa.[9]

In the majority of the experiments these were the only lesions found even in animals which had been under the influence of lead for two years and over (see, for example, experiments Nos. 22, 23, and 24), and even in those cases in which small areas of cellular infiltration are noted in the record it is very doubtful whether these can be ascribed to the lead-poisoning, because such lesions are not uncommonly found in the kidneys of untreated apparently normal guinea-pigs.*

This leaves six animals only (Experiments Nos. 11, 12, 16, 18, 25, and 27) that show more definite interstitial changes, and in four of these they are very slight indeed. The kidneys in these four cases did not show any gross lesions, and microscopically a few small areas were encountered in which small groups of tubules (probably adjoining sections through one and the same tubule) were in a state of collapse, and in which the connective-tissue between these tubules was very slightly proliferated. Even in the remaining two animals the condition is by no means striking.

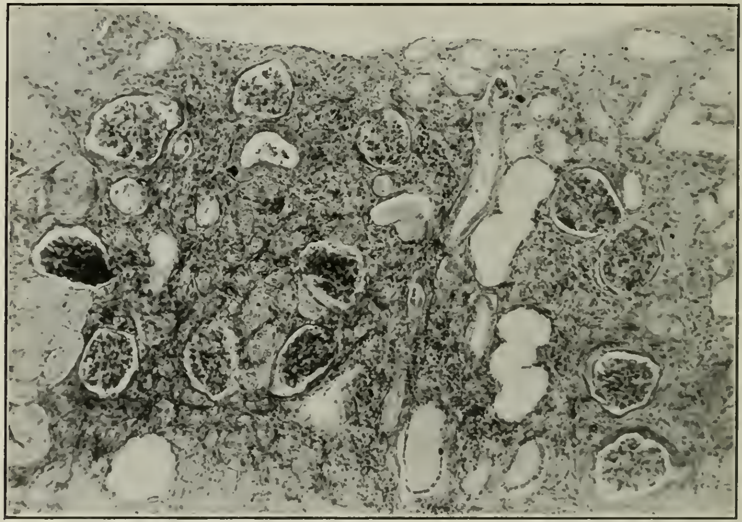

FIG. 4 (× 100).—Area of chronic nephritis with collapse of many tubules, dilatation of others, and capsular thickening of glomeruli. Experiment 27. Guinea-pig 69.

In Experiment 18 it is described as follows: "The kidneys show just visible, fairly regular pitting of the surface," and in Experiment 27, "kidneys fairly large, capsule non-adherent, surface coarsely and finely dimpled."

The most marked lesion found in the latter case[27] is shown in Fig. 4. The photomicrograph gives an idea of the slight depression on the surface, which is largely due to the collapse of the tubules. The slight thickening of the connective-tissue between them is also clearly brought out. At the base of the picture there is a moderate infiltration of the tissues with lymphocytes near some large vessels. The picture also shows a corresponding enlargement of other tubules in the vicinity, which is the usual thing in such cases.

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* See Ophüls. Occurrence of Spontaneous Lesions in Kidneys and Livers of Rabbits and Guinea-pigs, Proc. Soc. Exp. Biol. and Med., 1911, viii, 75.

The epithelium in these dilated tubules is partly atrophied, but in some the epithelial cells are evidently enlarged and proliferated.

The glomeruli in this figure are also of some interest, because they show the only lesion which was ever observed in them, and which occurs practically exclusively and constantly in foci of this character, namely, a fibrous thickening of the capsules which is usually rather moderate in extent and may be associated with a slight proliferation of the capsular epithelium.

None of the specimens show the slightest lesions in the bloodvessels.

The condition even in the most advanced case is in no ways similar to what one finds in the kidneys in human cases of chronic lead-poisoning. In them the involvement of the bloodvessels and of the glomeruli is a striking feature of the process, so much so that to all appearances the vascular lesions are primary, the kidneys in many cases being indistinguishable histogically from other forms of arteriosclerotic nephritis.

In a general way the lesions in the guinea-pig resemble histologically those observed in uranium nephritis in the same animals, although they are by no means so severe nor so extensive.

The reports in literature in regard to the action of lead on the kidneys of animals are very contradictory.* On the one hand we have Charcot and Gombault's[7] well-known report, according to which they found "granular" kidneys in 7 out of 15 guinea-pigs after continued administration of carbonate of lead by mouth. They claim that histologically the alterations found were identical with those in human lead nephritis. Their experiments lasted from two days to one year, and in one instance "distinctly granular" kidneys were found as early as the seventeenth day (Experiment 10). None of the later investigators have been able to repeat these experiments so successfully, if we except a rather general statement by Provost et Binet,[12] who after some rather unsuccessful preliminary attempts used Charcot and Gombault's method of feeding carbonate of lead to guinea-pigs on 25 animals; 17 of these survived the first month, most of them dying between the second and third months, One animal only lived six months. They say "lésions renales très accentuées chez la plupart d'entre eux, surtout quand l'intoxication avait duré longtemps," and make a similar statement in regard to fourteen rats that were treated similarly. It is to be regretted that they do not give their observations in greater detail. The experiment of Paviot[18] with carbonate of lead on six rabbits in which he found no gross lesions, but microscopically what he calls extensive sclerosis in two animals after about six months, are no more convincing, to my mind, especially as such lesions very commonly occur spontaneously in rabbits. What is particularly suggestive in this regard is the fact that the lesions in his cases appear to start in the pyramids and extend into the cortex radially as the spontaneous lesions in rabbits are likely to do.

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* At the end of the paper there is a list of the more important articles in historical sequence.

Coën and d'Ajutolo,[11] who experimented on rabbits with acetate of lead for at most 153 days, found only slight interstitial lesions, but believe that a longer administration of the poison might have produced a true renal cirrhosis, a surmise which hardly seems to be justified in the light of our experience. Jores,[26] who also used rabbits, found one small scar only in a rabbit that had been under experimentation for fourteen months and twenty days. All others who have paid any special attention to this point (Hoffa,[9] Oliver,[13] Stieglitz,[14] Annino,[16] Hirsch[20]) describe lesions no more marked than those which were observed in our own experiments.

The conclusions, therefore, seems to be justified that in the warm-blooded animals so far experimented on (guinea-pigs, rabbits, rats, cats, and dogs), chronic lead-poisoning produces in the kidneys primarily epithelial lesions, which condition eventually may be followed by a certain type of granular atrophy, due to collapse of groups of tubules, associated with some fibrous thickening of the connective-tissue between these tubules and of the capsules of the glomeruli in these areas, but that these changes always remain quite limited and are by no means constant. On the basis of my experiments I do not believe, as Jores[26] does, that these later lesions are at all more common in guinea-pigs than they are in rabbits. Certainly nothing has ever been reproduced in any of the animals mentioned which in any way resembles human lead nephritis, Charcot and Gombault's[7] statements to the contrary notwithstanding.*

The existence of epithelial lesions is acknowledged by all investigators, but even in this regard there are to be found certain minor discrepancies in the various reports concerning the exact form of degeneration of the protoplasm and of the nuclei of the cells involved. Annino[16] claims never to have seen any mitoses, which is certainly quite remarkable.

One curious feature in our experiments is the fact that whereas many of the other investigators have described calcareous deposits in the uriniferous tubules, often in large numbers, we have not encountered them in the kidneys of any of our animals, in spite of the fact that they were looked for carefully. They were first observed by Charcot and Gombault,[7] who say in regard to them, "On the cut surface one finds, especially in the pyramid, a large number of whitish, highly refractile dots and lines made up of solid masses of calcareous material, which infiltrates the tubules," and in another place, "One finds a certain number of the narrow branches of the loops of Henle filled with solid calcareous masses, the cellular structure of which becomes evident after decalcification." They are prominently mentioned and discussed by Prevost and Binet,[12] whereas Stieglitz[14] found them only rarely. Hirsch[20] and Hoddick[27] also mention them, others do not seem to have paid any special attention to this point. Paviot[18] did not find them in his few experiments on rabbits, and believes that Charcot and Gombault's[7] experimental results are largely due to the blocking of the tubules by the calcareous masses. These deposits are of great interest on account of the apparent close relation of chronic lead-poisoning in man to gout. The occurrence of similar calcareous deposits, containing urates also in the pyramids of the kidneys, is very common in such cases in man, and these sometimes are the only manifestation of the existence of a gouty diathesis. Whether the deposits in the animals also contained urates does not seem to have been ascertained. I may state here in passing that in spite of special attention to this point no evidences of gout was ever detected in any of our animals.

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* The statement which is sometimes found in literature that Leyden reported successful experiments of this character is entirely erroneous. In his paper read before the Verein f. innere Medicin at Berlin, March 19, 1883, and published in the Deutsch. med. Woch., 1883, ix, 185, Leyden reports a case of human lead nephritis, but makes no mention of any experiments whatever, nor does his pupil Muschold in his dissertation, Die Bleivergiftung eine Ursache chronischer Nierenerkrankung, Berlin, 1883.

The reports in regard to glomeruli and bloodvessels are also most curiously conflicting, which in itself suggests that they are by no means well marked or constant. A hyaline degeneration of the glomeruli has been described by Coën and d'Ajutolo[11] and by Stieglitz,[14] which we cannot confirm in our specimens. It is often difficult to make out exactly what sort of changes the authors allude to, because their statements are very general and few of them give any illustrations of the lesions encountered; but at best the lesions described appear to be slight, somewhat like those described above in our own specimens (slight fibrous thickening of capsules of Bowman, possibly associated with some atrophy of the glomeruli themselves, and a moderate proliferation of the epithelial lining of the capsules), and they are in no way comparable to the glomerular changes observed in human nephritis, either of the arteriosclerotic type or in well-marked glomerulonephritis.

So far as the bloodvessels are concerned, much emphasis is usually placed in reviews of the literature on Annino's[16] work, probably on account of a notice in the Virchow-Hirsch Jahresberichte (1894, I, 375), stating that he found "severe endarteritis which even lead to complete vascular obstruction." If one reads the original, however, and particularly the description of findings in the individual experiments, one discovers to his surprise that in most organs the arterial lesions were very slight indeed, possibly non-existent, except in the lungs, where Annino actually claims to have seen an endarteritis tending to occlusion.*

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* Annino[16] used 9 animals altogether in his experiments, 2 young dogs, 3 rats, 2 rabbits, and 2 guinea-pigs. The animals were observed for a few months only, one of the dogs lived longest, for seven months. None of them showed any important gross lesions.

Similar conditions in the pulmonary vessels have been noted by Stieglitz,[14] Greven,[25] and Jores,[26] but Jores very correctly pointed out that normally these vessels in rabbits, and he might have added in guinea-pigs, have very thick walls and a very narrow lumen, and that normally also the intima may be somewhat thicker and more cellular in places. Jores[26] still believes that he found a thickening of the intima which exceeded the physiological limits in those of the animals which had been exposed to the influence of lead longest, but even so he believes these slight alterations to be unimportant, and at the end of his paper he emphatically denies the importance of the vascular changes described by the above mentioned authors, and also by Maier and his coworkers. I fully agree with him on this point and wish to state positively that neither in my specimens have I ever seen anything resembling arteriosclerosis, nor am I at all convinced, from a careful study of the literature, that such changes have ever been produced in animals by chronic lead-poisoning.

The heart, so far as its weight is concerned, and the aorta were found to be entirely normal in all my animals.

THE LIVER. The lesions in the liver in chronic experimental lead-poisoning have attracted comparatively little attention, and yet from the results of my experiments it would appear as if they were really more important than those which occur in the kidneys.

Coën and d'Ajutolo[11] seem to have been the first to pay some attention to the liver. They describe primarily a "necrotic, granular degeneration of the liver cells," and later a chronic hyperplastic periangiocholitis. Since the latter, however, is commonly observed spontaneously in rabbits,* which animals they used for their experiments, this latter condition was possibly not the result of the lead-poisoning.

Oliver,[13] who also used rabbits, makes the following statement: "In the liver of animals and in the liver of lead-workers there will be found an atrophied, cloudy, or granular condition of hepatic cells, amounting at times to a true fatty degeneration. The columns of cells become irregular and slender, and thus become separated from each other by spaces of considerable size. For nearly all the specimens taken from human beings and ruminants these spaces between the individual hepatic cells and rows of cells were occupied by small round cells. There was an increase of connective-tissue elements, derived in all probability from the capillaries or the sheath which surrounded them. In other words, there was an intercellular cirrhosis not unlike that met with in congenital syphilis. The capillaries of the lobules were generally found to be overdistended, a condition observed nearer the centre than the periphery. Interstitial inflammation with degeneration of columns of liver cells was so generally present in all specimens that I cannot but regard this as a constant lesion, and as one likely to arise in the early stages of lead-poisoning." In the accompanying plates he shows the microscopic picture of a liver with well-advanced cirrhosis in a girl, aged eighteen years, who had worked only forty days in a lead-factory. His Fig. XXVIII, showing the microscopic picture of the liver of a rabbit with lead-poisoning, does not show any resemblance to the changes observed in our animals.

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* Ophüls, loc. cit.

Laffitte[15] emphasizes the hepatic changes in chronic lead-poisoning more strongly than any other author. He gave carbonate of lead to four rabbits by mouth for from one and one-half to five months and found no epithelial lesions except atrophy, but marked early interstitial lesions resembling those of cirrhosis. He further presents six human cases of cirrhosis in chronic lead-poisoning, two of which are personal observations. What has been said above in regard to spontaneous lesions in rabbits naturally applies here.

Annino[16] also describes degenerative lesions in the liver and some perivascular cellular infiltration and proliferation of the periportal connective-tissue.

Jores[26] found hematogenous pigmentation to a varying degree and marked hyperemia in the liver of his rabbits, but no other important changes.

The following interesting statement is made in Mallory's recent book on *Principles of Pathological Histology*:* "Lead salts given to rabbits and other animals in amounts just below the minimum fatal dose will produce in a few days a hyaline lesion in the liver cells similar in all respects to that found in the alcoholic cirrhosis of man. Some of the cells undergo necrosis and are removed by the digestive action of leukocytes. Regeneration of liver cells is shown by mitotic figures. This observation suggests that the so-called alcoholic cirrhosis of man may possibly be due to lead."

This is by far the most accurate observation so far recorded in literature.

It is astonishing that the severe gross changes in the liver which follow later in the stages of chronic experimental lead-poisoning and which may be well developed at the end of nine months (see our observation to 14) have apparently never been recorded before.

The initial lesion which has been constantly found in all our cases in which a microscopic examination was made is, as Mallory states, a peculiar hyaline degeneration of the protoplasm of the liver cells associated with pyknosis of the nuclei, eventually terminating in necrosis. The change is clearly shown in three cells in the centre of Fig. 5. The degenerated cells occur either singly or in small groups of two to three cells without any characteristic distribution so far as could be made out. Eventually the remnants of the cells are either absorbed or may be removed by leukocytes, as stated by Mallory. New cells to take their place are produced by mitosis.

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* F. B. Mallory, The Principles of Pathological Histology, Philadelphia, 1914, p. 507.

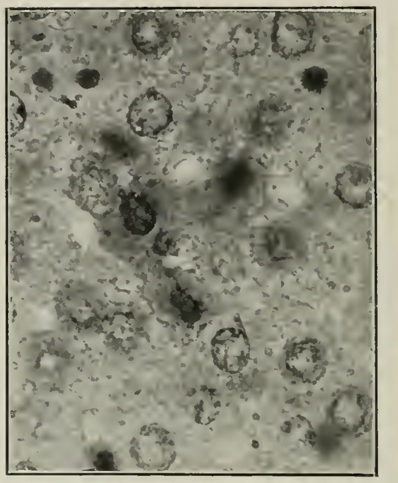

Fig. 5 (× 750).—Hyaline degeneration of small group of liver cells with pyknosis of neuclei. Experiment 3. Guinea-pig 02.

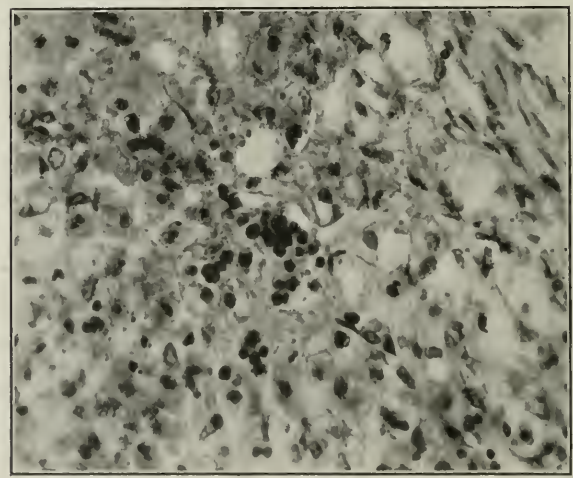

Fig. 6 (× 350).—Fatty degeneration and necrosis of large central group of liver cells with beginning collapse of tissue. Fibrous thickening of capsule. The cells with deeply staining nuclei in centre of field are situated in the central vein of a lobule. Experiment 14. Guinea-pig 3.

In the end these degenerative lesions which may be associated with fatty degeneration may become more and more extensive, so much so as to destroy large parts of the liver tissue, as shown in

Fig. 6, in which practically all the cells in the field are either in a state of severe degeneration or actually necrotic and disintegrating.

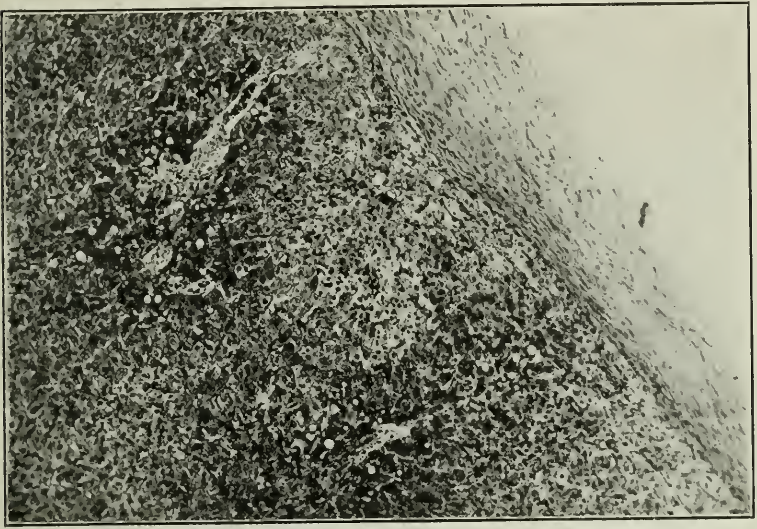

Fig. 7 (× 100).—The same specimen taken with a low power, showing distribution of lesion and marked chronic perihepatitis. Experiment 14. Guinea-pig 3.

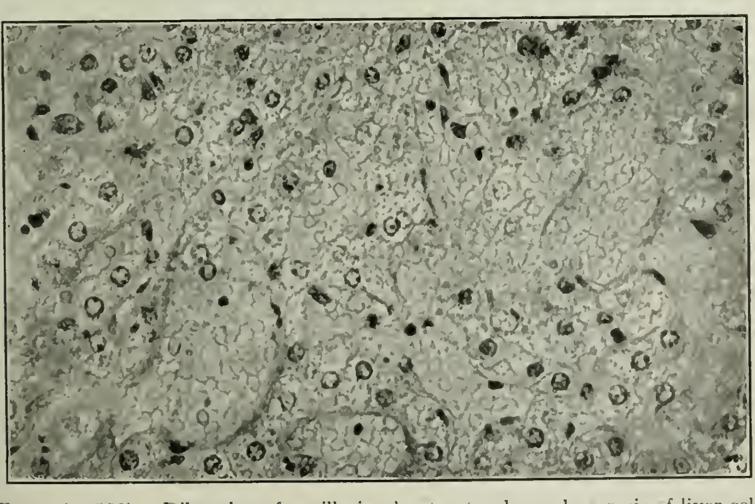

Fig. 8 (× 350).—Dilatation of capillaries due to atrophy and necrosis of liver cells. Experiment 16. Guinea-pig I.

The removal of the dead liver cells naturally causes a tendency to collapse on the surface, and in the interior of the organ a tendency to dilatation of the capillaries in the same way, as one observed it in the red parts of a human liver in subacute yellow atrophy.

Fig. 7 is a photomicrograph of the same lesion shown in Fig. 6 at a lesser magnification, and brings out more clearly the peculiar localization of it. The dilatation of the capillaries in the interior of the organ is well shown in Fig. 8, whereas the tendency to collapse is clearly observed in Fig. 9, in which there are also some large areas of capillary dilatation.

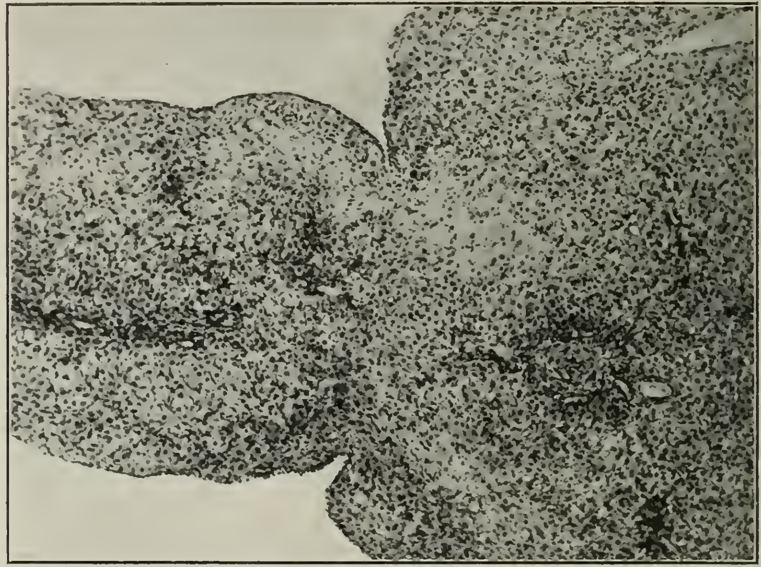

Fig. 9 (× 100).—Extensive areas of degeneration and necrosis of liver cells with dilatation of capillaries and deep retractions due to collapse. Experiment 22. Guinea-pig 33.

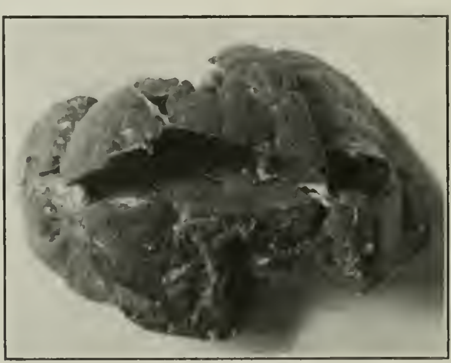

Fig. 10.—Gross appearance of liver of guinea-pig 54 (Experiment 21), showing irregular fibrous thickening of capsule, finely granular surface, and large irregular depressions.

The condition is similar to subacute yellow atrophy. Sometimes it involves the organ diffusely, as in observation No. 14, in which the liver remained fairly smooth; but more commonly it is localized in circumscribed spots, and in this way produces first a more or less regular pitting of the surface. Later there is a markedly granular appearance with shrinkage, which in the gross strongly suggests cirrhosis (Figs. 10 and 11).

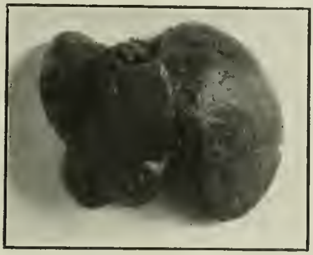

Fig. 11.—Gross appearance of liver of guinea-pig 35 (Experiment 17), showing finely granular surface and dimpling.

There is this important difference, however, that there is little if any proliferation of the connective-tissue associated with the process, at least in guinea-pigs. Fig. 12 is taken from the specimen in which the interstitial lesions were most clearly developed in an animal which had survived for one year and eleven months (observation No. 20). The later animals (Nos. 21, 22, 26), in all of which the hepatic lesions were well developed, showed less proliferation

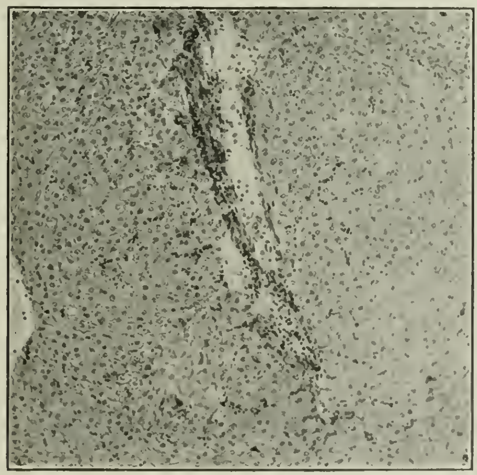

Fig. 12 (× 100).—Cellular infiltration and fibrous thickening of periportal connective tissue. Experiment 20. Guinea-pig 24*a*.

in the periportal connective-tissue, which in observations No. 22 (two years and two months) and No. 26 (three years and one month) amounted to no more than a slight cellular infiltration. It does not appear to be likely, therefore, that the lack of connective-tissue formation was due to insufficient time for its development or that a prolongation of the experiments, if possible, would have brought more striking results in this regard.

Kretz* defines cirrhosis as a "focal recrudescent chronic atrophy modified by intermittent degeneration of the parenchyma." It appears to me that his definition applies much more correctly to the changes observed in these guinea-pigs than to cirrhosis in man, and that it seems evident that such a process cannot in itself explain the abundant connective-tissue formation in human cirrhosis. And yet the process in our experiments would seem to be specially suitable to reproduce conditions resembling human cirrhosis because it is associated with severe anemia, a combination to which Kretz* also alludes in his paper. It is worthy of note that in spite of the constant occurrence of degenerative lesions of moderate degree in the livers of all guinea-pigs examined, and of slight pitting in all animals after the ninth month, severe changes were found to be comparatively rare. They were present in Cases Nos. 14, 16, 17, 20, 21, 22, 26 in seven out of twenty-eight animals. Of the three cases which lasted over three years, one only showed advanced changes in the liver.

The following is a short *resumé* of the more interesting experiments:

14. Guinea-pig 3. The liver is much reduced in size, measuring 5 x $3\frac{1}{2}$ x 2 cm. (normal measurements at least 7 x $4\frac{1}{2}$ x $2\frac{1}{2}$ cm.). The capsule is slightly thickened diffusely, and in places there is a very marked fibrous thickening of the same (Fig. 7). The surface of the liver is smooth, but the shape of the organ is much distorted. The sharp edges are all rounded, and here and there along the anterior now rounded border one sees rather coarse nodules with fairly deep rounded depressions between them. The microscopic appearances of the liver tissue are shown in Figs. 6 and 7. There are many large areas of fatty degeneration and necrosis in which one finds considerable granular hematogenous pigment. The periportal connective-tissue is cellular, slightly increased in amount, and sends slender projections to the thickened capsule. The spleen is large, over twice normal size; marked perisplenitis; few drops of clear fluid in abdomen; chronic pericarditis.

16. Guinea-pig 1. The liver is slightly reduced in size ($5\frac{1}{2}$ x $4\frac{1}{2}$ x $2\frac{3}{4}$ cm.). The capsule is slightly thickened. The surface is finely and evenly granular, showing dark-red spots about 1 mm. in diameter with a grayish depressions between them. On the lower surface

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* Lebercirrhose, Verh. der Deutsch. path. Ges., 1904, viii, 54.

of both lobes there are some deep irregular fissures. Microscopic sections show large areas of fatty degeneration and necrosis with marked dilatation of capillaries (Fig. 8) and areas of collapse on the surface of the liver. No hematogenous pigment was found in the liver. The periportal connective-tissue is slightly thickened and infiltrated with lymphocytes. The spleen was of about normal size. Marked, slightly hemorrhagic, ascites; chronic pericarditis; serofibrinous pleurisy.

17. Guinea-pig 35. The liver is of nearly normal size, measuring 7 x 5 x 2½ cm. The surface is distinctly granular (Fig. 11). The granules measure about 1 mm. in diameter. In addition there is some deep pitting, more especially on the lower surface of the liver, where there are many deep fissures. Sections show large areas of fatty degeneration and necrosis, with collapse of tissue on the surface, causing the granular appearance and the pitting. Slight cellular infiltration of the periportal connective-tissue; slight perihepatitis; marked ascites; chronic pericarditis; chronic pleurisy with effusion; anasarca.

20. Guinea-pig 24a. The liver is much shrunken, measuring 5¾ x 4 x 2 cm. The capsule shows a marked irregular fibrous thickening. The shape of the liver is much altered, much like the liver of Guinea-pig 3. The edges are rounded off and the various lobes firmly adherent to one another. The surface shows coarse nodules with deep furrows between them. Sections show large areas of fatty degeneration and necrosis with dilatation of capillaries and collapse of the liver tissue. The periportal connective-tissue is normal except for a slight cellular infiltration. The spleen is large (3½ x 1¾ x ¾ cm.). Marked ascites; hemorrhagic pericarditis; hemorrhagic pleurisy.

21. Guinea-pig 54. The liver is considerably reduced in size, measuring 6 x 4 x 2 cm. The capsule shows a marked irregular fibrous thickening. The surface is uneven and distinctly finely granular, There is also much deep pitting (Fig. 10). Sections show many large central areas of fatty degeneration and necrosis, with collapse of liver tissue and dilatation of capillaries. Much hematogenous pigment is found in the capillary endothelium. In this guinea-pig the cellular infiltration and proliferation of the periportal connective-tissue is more marked than in any of the others as shown in Fig. 12. The spleen is large, 4 x 2½ x 1 cm. Much ascites; hemorrhagic pericarditis; serous pleurisy; anasarca.

22. Guinea-pig 33. The liver is slightly reduced in size, measuring 6½ x 4½ x 2½ cm. The capsule is slightly thickened in a few places. The surface is distinctly granular, the granules measuring about 1 mm. in diameter. There is some deeper pitting on the left side above and below. Sections show fatty degeneration and marked atrophy of the epithelial cells in the centres of the lobules, with dilatation of the capillaries. The granules on the surface are due

to collapse of liver tissue. In the periportal connective-tissue one finds a slight cellular infiltration. The spleen is moderately enlarged, about twice normal size. Little ascites; hemorrhagic pericarditis; serous pleurisy.

26. Guinea-pig 46. The liver is much reduced in size, measuring 6 x 4 x 2 cm. The capsule is much thickened and the upper surface of the liver is attached to the diaphragm. All lobules are adherent to one another and the shape of the organ is much altered, much like the livers of guinea-pigs 3 and 24*a*. The cut surface of the right side shows large areas of necrosis and softening. Microscopic sections show the usual lesions and in addition large bacterial necrosis. The spleen is small, firmly attached to the fundus of the greatly dilated stomach by the thickened capsule. Ascites; hemorrhagic pericarditis; serofibrinous pleurisy.

What makes these changes even more deceptively like human cirrhosis is the constant association in them of severe hepatic disease with accumulations of fluid in the peritoneal cavity and with chronic inflammatory lesions of the serous membranes, more particularly of the peritoneum in the upper part of the peritoneal cavity, which are so commonly observed in human cirrhosis.

The possibility of lead as an etiological factor in human cirrhosis as suggested by Mallory has been discussed by few clinical writers. Aubry reported two cases of Coutenot's in 1865, which in literature are usually recorded twice, both under Aubry and Coutenot's names.[36] In one of these cases a typical cirrhosis was found at autopsy in a girl suffering from chronic lead-poisoning. Laffitte, as stated, has collected six cases of this kind, and Oliver[37] seems to favor the idea that lead is an important factor in certain cases of cirrhosis. Potain[38] also believes that chronic lead-poisoning is definitely though rarely a cause of cirrhosis, and cites some cases in support of his view. He believes that the prognosis of this form is unusually good. It has been suggested that alcoholic beverages are commonly adulterated with lead, still the use of sugar of lead for clearing and sweetening the wines has been long discarded. On the whole there seems to be little clinical evidence so far to connect human cirrhosis with chronic lead-poisoning.

In our service among twenty-five necropsies on painters who had all shown more or less evidence of lead-poisoning, only one case of advanced cirrhosis was observed, and this one in a man who except for some anemia did not show any other evidences of lead-poisoning. In addition there were in this series four cases of slight beginning cirrhosis, which would hardly be suggestive of a more common occurrence of cirrhosis in lead workers. It may be interesting to note here that many of the livers in the more marked cases of chronic lead-poisoning did show some degenerative lesions in the epithelium, resembling those observed in the majority of our guinea-pigs.

As a unique finding in our series of animals, I wish to call attention to the severe myocarditis observed in Case 28 (guinea-pig No. 12), of which photomicrograph 13 gives a representation. This animal happens to be the one longest surviving (for three years and ten months). There were present in addition in this animal marked degenerative and slight interstitial lesions in the kidneys, moderately advanced lesions in the liver, also some ascites, chronic pleurisy with hydrothorax, and a slight chronic pericarditis with effusion. No similar lesions of the heart muscle were discovered in any of the other animals, even in those with much more marked degrees of pericarditis.

THE SEROUS MEMBRANES. The serous membranes have received even less attention than the liver in chronic experimental lead-poisoning. The frequency of pericardial lesions is commented upon by Charcot and Gombault[7] in the following statement: "At autopsy of the animals we were impressed by the condition of the pericardium, which we found diseased in 7 out of 15 cases. There was found in the serous cavity an effusion, sometimes simple, sometimes bloody, associated with the formation of abundant false membranes on the surface of the two layers of the pericardium." Their records of the individual cases show that this condition eventually leads to marked fibrous thickening, more especially of the visceral layer, and sometimes to adhesions. They did not observe any changes in pleura or peritoneum except in Observation 9, in which they note the presence of an enormous "blood-clot in the peritoneum," without further discussion. Prevost and Binet[12] also noticed pericarditis in 8 out of 25 guinea-pigs, which were given carbonate of lead by mouth, like the animals in the experiments

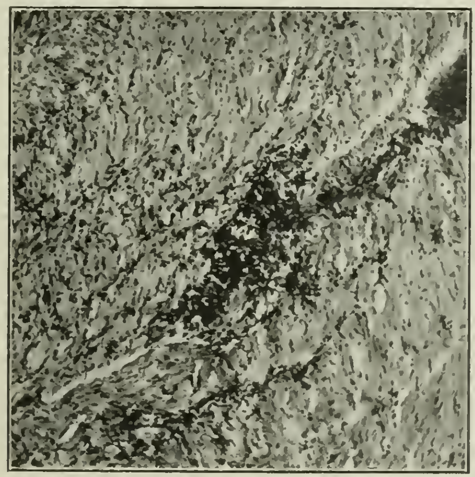

FIG. 13 (× 100).—Myocarditis. Experiment 28. Guinea-pig 12.

of Charcot and Gombault.[7] Stieglitz[14] observed pericarditis in two of his animals. Paviot[18] found a localized gelatinous pericarditis in one of his rabbits. This animal also had been given carbonate of lead in large doses. These are the only references to experimental observations of this kind which I have been able to find in literature and they seem to have attracted practically no attention. Our clinical knowledge in regard to this subject is still more rudimentary. Galvagni* seems to be the only one who has discussed the subject at some length. He says: "In the last year I had the opportunity to observe in my clinic at Modena two cases, which induce me to believe that inflammatory lesions in the peritoneum, more especially in the mesentery, may be a possible result of chronic lead-poisoning." One of these cases came to autopsy, and Foà found perisplenitis; perihepatitis, with total adhesion of the stomach, of the liver, and of the spleen to the diaphragm; total sclerosis of the great omentum; chronic sclerotic mesenteritis with retraction of all loops of the bowel; sclerosis of the solar plexus, etc.

The constancy and extent of the lesions in our guinea-pig is certainly remarkable. Even in the more acute form of the intoxication, especially when the animals receive large doses of lead, small, often hemorrhagic, effusions take place into the serous cavities, as is shown in Experiments Nos. 1 to 5 inclusive. The next series of animals that were given much smaller amounts (Nos. 6 to 11) and also cases 12 and 13, in spite of large doses, show normal serous membranes; but from there on, with the one exception of Experiment 18, the animals all have marked lesions in their serous membranes.

14. Guinea-pig 3 had a few drops of clear fluid in the peritoneal cavity. In the upper part of the abdomen the peritoneum is slightly thickened. The thickening is quite diffuse and somewhat varying in intensity. The capsule of the spleen is thick and fibrous. The parietal pericardium is quite thick and white, and there are some white spots on the visceral layer. The pleuræ are moist, otherwise normal. Smears of the serous membranes show many red-blood corpuscles, many of them nucleated, some megaloblasts, few endothelial cells and lymphocytes, few polymorphonuclear leukocytes. No bacteria were found in spite of the use of various staining methods and in spite of careful search.

15. Guinea-pig 2 had a marked ascites, slight chronic perihepatitis, and slight chronic pleurisy.

16. Guinea-pig 1 had a marked, slightly hemorrhagic, ascites. The peritoneum was slightly thickened, smooth, hyperemic. There were old adhesions between spleen and stomach and between liver and kidney. Slight perihepatitis. Much clear fluid and several thick flakes of fibrin were found in the pleuræ. The lungs were col-

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* Galvagni, Sopra un caso di mesenterite in uno saturnino, Riv. Clin., 1884, iii, 23.

lapsed. The pericardium was filled with fluid blood. It was somewhat thickened and the surface slightly rough. Smears of serous membranes showed red blood corpuscles, some lymphocytes, and large phagocytes. No bacteria were found. Hyperemia and edema of subcutaneous fat.

17. Guinea-pig 35 had a slight chronic pericarditis and a marked ascites and hydrothorax, without marked change in peritoneum or pleura, except a slight chronic perihepatitis. Marked general anasarca.

18. No lesions in serous membranes.

19. Guinea-pig 14 had a beginning chronic pericarditis only.

20. Guinea-pig 24*a* had about 10 c.c. of clear fluid with small flakes of fibrin in the peritoneum. There was present a marked irregular thickening of the parietal and visceral peritoneum, including the capsules of liver and spleen. The pericardium contained some slightly hemorrhagic fluid. It was covered with fibrin, and there were some recent adhesions. Much hemorrhagic fluid and much fibrin were found in both pleuræ. Both lungs were collapsed.

21. Guinea-pig 54 had marked ascites. The liver was covered with thin, easily detached shreds of fibrin. Both pleuræ were filled with clear fluid. The lungs were collapsed. Few drops of blood filled the pericardium. Very marked general anasarca.

22. Guinea-pig 33 had few drops of clear fluid in peritoneum. In several parts of the upper peritoneal cavity, especially on the surface of the liver, one noticed thin, non-adherent fibrinous deposits. The peritoneum was also slightly thickened all over. Both pleuræ were filled with clear liquid and the lungs were collapsed. The pericardium contained few drops of pure blood.

23. Guinea-pig 34 had few drops of fluid in peritoneum. The visceral pericardium was slightly thickened.

24. Guinea-pig 31 had little fluid in the serous cavities and a slight pericarditis.

25. Guinea-pig 32 showed but a slight pericarditis.

All three of these animals (Nos. 23, 24, 25) were extremely emaciated females, whereas the strong, well-nourished animals, more especially the males, were the ones which showed the marked lesions in the serous membranes.

26. Guinea-pig 46 had 30 c.c. of slightly bloody fluid in the peritoneum. The peritoneum, especially in the upper part of the abdominal cavity, was moderately thickened. Recent fibrinous deposits were found over the stomach and liver. Thick fibrous bands developed between stomach and mesentery, which had caused a partial strangulation of the small bowel. The duodenum was also surrounded by the adhesions. The stomach above the obstruction was greatly distended. The spleen was attached to the fundus of the stomach and the liver to the diaphragm. The pleuræ were covered with fibrin and contained little fluid. Few drops of bloody

fluid were found in the pericardium. In this case the diseased liver had been invaded by colon bacilli, which had caused extensive bacterial necrosis.

27. Guinea-pig 69 showed nothing but a slight pericarditis.

28. Guinea-pig 12 had a marked ascites, much fluid in both pleuræ, and some fluid in the pericardium. Both the parietal and visceral pericardium were slightly thickened.

The lesions in the serous membranes are evidently closely connected with the lead anemia. As a result of this condition the capillaries become more permeable, not only in the serous membranes, but all through the bodies of the animals, as is shown by the quite common occurrence of a general edema (Experiments 16, 17, 21). In all animals except those which were extremely emaciated the tissues were found not only hyperemic, but distinctly moist. It is possible that the hydremic condition of the blood itself contributes to the liability to leakage from the bloodvessels.

The character of the fluid which exudes into the serous cavities varies greatly, but it is always more or less hemorrhagic and has a tendency to coagulate on the serous surfaces, forming false membranes, which are later organized and lead to thickenings and adhesions. Fig. 7 shows a marked thickening of the capsule of the liver, produced in this way. In Fig. 10 similar capsular thickenings are represented in their gross appearance. In some of the cases the capsular thickening of the liver was so diffuse and well marked that the appearances of a "Zuckergussleber" were closely reproduced.

The danger of adhesions from this source is well shown in Case 26, in which a strangulation of the upper part of the small bowel had resulted from them.

In the pericardium almost pure blood was found quite commonly, and it is interesting to note that this blood was often unusually rich in nucleated reds, and sometimes contained large megaloblasts.

The effusions undoubtedly have somewhat of an inflammatory character, as evidenced by their tendency to coagulation and by the presence in them of rather large numbers of lymphocytes, and occasionally even polymorphonuclear leukocytes. Several specimens were carefully examined for bacteria in smears and culture, but none were found except in the case in which a bacterial infection had been caused as a result of the strangulation.

How far similar conditions occur in human cases of chronic lead-poisoning is still unknown. I have already referred to Galvagni's* case. In our series of 25 painters, pericarditis occurred only twice, both in cases of advanced chronic lead-poisoning. One of the cases showed a typical lead palsy, and both had lead anemia and severe progressive nephritis, marked arteriosclerosis, and some cardiac hypertrophy. In the one case (VIII, 34) the pericardium contained about 200 c.c. of a dark-red fluid with large, red, soft flakes of fibrin. It was covered with a moderately thick layer of grayish-red fibrin, which was firmly attached to the pericardium. No bacteria were found in a culture taken from the pericardium. Peritoneum and pleuræ were normal.

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* Galvagni, loc. cit.

In the other case (V, 50) about one tablespoon of slightly bloody fluid was found in the peritoneum. The pericardium contained about one-half teaspoonful of slightly turbid fluid. Both layers of the pericardium were covered with a thin layer of fibrin which could be detached easily. In the pleuræ over a liter of fluid was found on both sides, the fluid on the left side being slightly hemorrhagic. Unfortunately no bacteriological examination was made of the serous cavities in this last case.

In spite of the slight indications at the present time of a clinical significance of these experimental findings it may very well be that more careful attention directed to the possibility of such occurrences will reveal them much more commonly than would appear at the present time, and the diagnosis of chronic lead-poisoning may clear up some of those puzzling cases of polyserositis or polyorrhomenitis which have been described in literature, especially by Italian clinicians, and may contribute to the proper understanding of such conditions as Pick's pseudocirrhosis and Curschmann's "Zuckergussleber."

Conclusions. 1. Chronic lead-poisoning in guinea-pigs produces severe degenerative changes in the epithelium of the kidneys and of the liver, leading to necrosis. These destructive lesions are partly compensated for by constant regeneration.

2. In the kidneys these lesions may eventually cause collapse of certain groups of tubules associated with moderate proliferation of the connective tissue and some chronic inflammatory changes. The glomeruli in these foci usually show a fibrous thickening of the capsule. In exceptional instances the defects produced in this way are large enough to cause a somewhat granular gross appearance of the organs.

3. In the liver large areas of collapse occur much more frequently, so much so that marked irregularity of the surface resembling that observed in human cirrhosis is quite common. The connective-tissue proliferation associated with this process is extremely limited. The condition, therefore, cannot well be classified as a cirrhosis, but should be designated as a chronic focal atrophy.

4. Chronic lead-poisoning in guinea-pigs produces general increased permeability of the bloodvessels leading to the production of effusions, usually of a hemorrhagic character, into the serous cavities. These are most commonly observed in the pericardium, but the pleuræ and the peritoneum are often also involved in the process. False membranes are apt to form on the surface of the serous membranes, and their organization leads to the development

of the picture of a chronic polyserositis with fibrous thickening and sometimes adhesions. If this condition is more especially localized in the pericardium there may be the appearances of a pericarditic pseudocirrhosis; if more in the capsule of the liver, that of a "Zuckergussleber" may be reproduced.

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APPENDICITIS AS A SEQUELA OF TONSILLITIS.

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The occurrence of appendicitis as a sequela of tonsillitis has received less attention from clinicians in America and Great Britain than its practical importance warrants. Most of the standard works on medicine and surgery make no reference to it, and it is seldom noticed in current medical literature. This is the more remarkable, since the importance of the tonsil as the port of entry of many forms of systemic infection, and as the starting-point of disease in distant organs, has been well established in recent years in numerous contributions by recognized authorities. In this connection one need only enumerate general sepsis, acute rheumatism, chorea, endocarditis, pneumonia, pleurisy, empyema, meningitis, nephritis, urethritis, orchitis, thyroiditis, and cholecystitis, all of which have been definitely traced to acute tonsillar infections.

About a year ago a patient entered my service in St. Michael's Hospital, a young woman, who developed an abscess in the upper lobe of the right lung a week after an operation for removal of the tonsils during the subsidence of an acute angina.

The relationship between acute rheumatism and appendicitis has frequently been noted, and when one recalls how often tonsillitis precedes the former, the etiological connection of tonsillitis with appendicitis is more readily apparent. To Sir James Grant, of Ottawa, is due the credit of reporting in 1893, the first modern instance of the association of appendicitis and rheumatism.[1]

The same year Kelynack directed attention to the occurrence of appendicitis secondary to tonsillitis.[2]

In Europe the association of the two diseases has been more systematically studied from both the experimental and clinical stand-points, and consequently more generally recognized by the medical profession as a whole. The similarity in structure between the tonsil and appendix has frequently been pointed out and given as an explanation of their liability to similar infections. While the general trend of opinion among those who have studied the question is to recognize the etiological association of the two diseases, there is considerable diversity of view as to its frequency and the route of transmission of the infection. The experimental and clinical investigation of the latter has elicited much information bearing upon the pathology of appendicitis, especially as to whether the disease is due to a local infection from the bowel or to a hematogenous infection, with secondary localization in the lymphoid tissue of the appendix.

Adrian, in 1901,[3] succeeded in producing appendicitis in rabbits by the intravenous injection of staphylococci, streptococci, pneumococci, B. typhosus, B. coli, B. anthracis, and the tubercle bacillus. He regards the appendix as a point of election for the localization of general infections.

Subsequently, Tedesco[4] investigated experimentally the significance of tonsillar infection, using streptococci, staphylococci, and B. anthracis. He concluded that pyogenic germs from the pharyngeal ring can in rabbits lead to embolic processes in the parenchyma of the appendix, and that it is therefore possible for hematogenous infection to produce characteristic follicular disease of the appendix.

Mori[5] concludes that appendicitis may originate by way of the blood channels.

Kretz[6] believes that almost every case of appendicitis is in causal connection with angina through hematogenous infection.

The conclusions of these authorities have been called in question by Ghon and Namba[7] as the result of their experiments, as well as by Aschoff,[8] Oguro,[9] and others.

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[1] New York Med. Record, 1893, l, 609.

[2] A Contribution to the Pathology of the Vermiform Appendix, London, H. K. Lewis, 1893.

[3] Mitteilungen aus der Grenzgebiete d. Med. u. Chir., Band vii, S. 407.

[4] Experimentelle Beiträge zur die Aetiologie der Epityphlitis, Deutsch. Zeitschr. f. Chir., 1904, Band lxx.

[5] Eine experimentelle Arbeit über die Aetologie d. Epityphlitis, Deutsch. Zeitschr. f. Chir., 1904, Band lxx.

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Other more recent investigations and clinical reports, however, recognize the possibility of hematogenous infection and the importance of tonsillitis in relation to appendicitis.

Schroetter[10] thinks that an etiological connection between angina and appendicitis has been established, and that this is confirmed by the prevalence of appendicitis a few weeks after the changeable seasons, when angina and throat troubles are especially common.

Kelly[11] recognizes the relationship of appendicitis to tonsillitis, and states that in the surgical clinic of the Johns Hopkins Hospital there were 3 instances of its occurrence out of 91 cases of simple acute appendicitis.

Very convincing evidence in favor of the hematogenous origin of appendicitis has been brought forward by Poynton and Paine,[12] who believe that they have furnished almost conclusive proof that appendicitis may result from streptococcal invasion through the blood stream from a follicular tonsillitis.

Oguro thinks there is no doubt that hematogenous infection does occur in some cases, but less frequently than Kretz maintained. Boit and Heyde[13] express a similar opinion.

Heile[14] does not deny the possibility of hematogenous infection, but it seems to him more natural and simple to assume that the infective agent reaches the appendix and peritoneum from the intestines.

Haeberlin[15] thinks there is no doubt that hematogenous infection occurs after angina and scarlet fever, but that the number of cases in which it plays a role is very limited.

Heyde[16] reports a case of appendicitis following angina, and while he believes a hematogenous origin is uncommon, yet the importance of angina as a predisposing factor should be recognized.

Rèthi[17] says that recently it has been recognized that the tonsils comparatively often form the starting-point of general infections, including appendicitis. An instructive case is mentioned by Deaver of an appendicular abscess following an attack of diphtheria. L. Herdelet[18] reports two cases of appendicitis following tonsillitis. Many other cases might be referred to, but sufficient data have been brought forward to indicate the general trend of opinion, and the wide recognition of the association of tonsillar infections with appendicitis which has occurred in recent years.

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[7] Zur Frage über die Genese der Appendicitis, Beitr. z. Path. Anat., 1911, Band lii, S. 120.

[8] Die Wurmfortsatzentzundungen, Jena, 1908.

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[10] British Med. Jour., 1907, i, 534.

[11] Appendicitis and Diseases of the Vermiform Appendix, 1909, p. 150.

[12] Further Contribution to the Study of Rheumatism, Lancet, 1911, ii, 1189; also The Etiology of Appendicitis as a Result of Infection, Lancet, 1912, ii, 439.

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[15] Zur Entstehung der Wurmfortsatzentzundungen, Deutsch. med. Wchnsch., 1909, xxxix, 394.

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Tedesco[19] says he has produced embolism and necrosis of the appendicular follicles experimentally in rabbits. He further states that if appendicitis is immediately preceded by tonsillitis, rapid necrosis of a follicle in the appendix, with perforation or gangrene, is to be anticipated, and therefore operation should be performed early.

Tedesco and also others have referred to the tendency which these cases following tonsillar infection have to develop extremely acute symptoms.

He says that when a staphylococcic infection becomes generalized it is likely to prove fatal. This, however, is by no means an invariable result.

It would therefore appear to be established on experimental as well as clinical data that a hematogenous origin of appendicitis does occur, a fact of much importance in explaining the unusual course at times taken by the latter disease. The clinical relationship of appendicitis and tonsillitis, however, does not depend for its acceptance upon the theory of the hematogenous origin of the appendicular infection. It has been shown that appendicitis can be produced in rabbits by feeding pathogenic bacteria (Chastenet),[20] so that the possibility of infection from the tonsil by way of the alimentary tract is readily apparent.

Some seven years ago my attention was first directed to the occurrence of appendicitis as a sequela of tonsillitis by a case which came under my observation, the history of which is briefly as follows:

H. T., aged nineteen years, student. Father and mother both living and well, aged seventy-five years. They had ten children, all living and well. One brother and one sister had suffered from stomach trouble, with much distention at times, the brother having had a gastro-enterostomy performed by Dr. Stiles, of Edinburgh. The patient, though not robust, had always had good health.

On January 10, 1907, he felt chilly, "out of sorts," had slight headache, general pains, anorexia, and sore throat. When I saw him the next day, examination showed that the tonsils were enlarged and that there was follicular inflammation. The pharynx, fauces, soft palate, and uvula were also swollen, dusky red in color, and there was a slight sticky exudate on the pharynx. Temperature, 102°; pulse, 100.

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[18] Gaz. Hebd. Soc. Méd. de Bordeaux, April 12, 1914 (British Med. Jour., June 6, 1914).

[19] Wiener med. Wchnsch., January 9, 1914, p. 82.

[20] Thèse de Paris, 1897.

Rest in bed, gargles, and aspirin were prescribed. A culture taken from the throat showed Staphylococcus pyogenes aureus.

On the following day the condition of the throat was considerably better; the temperature was 102.5° and the general condition remained much the same. On January 13, I was called to see him at 4 A.M., owing to the development of severe epigastric pain, gastric distention, and belching of gas. There was some tenderness over the epigastric and left hypochondriac regions, and the stomach was so distended that the outline of the great curvature was plainly visible, moving up and down with respiration. The bowels had been moving freely. Temperature, 100°; pulse, 84. There was absolutely no pain, tenderness, distention, or rigidity over other areas of the abdomen. The throat condition had greatly improved. The pain disappeared in a short time, and for two days the patient was apparently much better; the throat had cleared up. Evening temperature, 98.1°; pulse, 80.

On the evening of January 15, there was a recurrence of pain, and he was sent to the hospital on January 16. On admission, at 10 A.M., the temperature was 98°; pulse, 84. Gastric distention, with retching, but inability to vomit, had recurred, and the patient looked ill, out of proportion to his other symptoms.

Dr. G. A. Bingham saw him in consultation at 4 P.M. The temperature was 97.3°; pulse, 84; respirations, 18. There was distention in the epigastric region, but no pain, tenderness, rigidity, or distention elsewhere. He considered operation unwarranted. The throat was practically well.

During the night general abdominal pain, tenderness, and distention developed. The temperature increased to 99.2°; the pulse to 140. The condition unfortunately was not reported to me until my arrival at the hospital in the morning. The patient at that time had all the signs of a generalized peritonitis. An operation was performed and a gangrenous appendix found, with a generalized peritoneal infection. The patient died the same evening. No autopsy was obtained.

Urinalysis on the morning of operation was negative; leukocytosis, 30,000.

The case was so unusual in its course, so distressing in its outcome, and presented so many puzzling features, that I have since followed the subject with much interest.

Dr. Lorne Main, of Dundas, has kindly supplied me with notes of another case, as follows:

J. W., aged twenty-two years. The patient was a robust young man, weighing 190 pounds. He had had an attack of gonorrhea three years previously and a syphilitic infection one year before the illness to be discussed. On March 4, 1911, he sought treatment for acute follicular tonsillitis. His temperature was 103.5°; pulse, 96. He complained of slight pain and tenderness in the right iliac region, which had, however, disappeared by the next day. Under the usual treatment his temperature became normal on March 8, although he was not allowed out until March 14. He felt very well, and went out for a walk. The tonsillitis had entirely subsided. About 9.30 in the evening he complained of headache and feeling tired; the temperature was normal; pulse, 80. On the next day, March 15, he was about the house; pulse and temperature both normal. The bowels had not moved for two days. At 3 A.M. on March 16, he was attacked by severe abdominal pain.

Dr. S. Cummings operated at 3.30 P.M. There was a gangrenous appendix, with what appeared to be gangrenous areas in the adjacent portions of the small and large bowel. The patient died at 1.30 A.M., March 17.

Other observers have reported cases in which the tonsillitis preceded the appendicitis by only a few hours, and it has been noted that rheumatism may develop coincidently with or in some cases follow the onset of appendicitis.

In both these cases a remarkable feature was the latency of symptoms referable to the appendix. The absence of fever or increase of pulse rate until the sudden development of fulminating symptoms may also be noted. In both cases a gangrenous appendix was found within about twelve hours after the onset of symptoms which might be definitely referred to the appendix. In my case the early pain and tenderness were both referred to the epigastric and left hypochrondriac regions, especially the latter, and the stomach showed extreme distention. Dr. Bingham and I both attributed the epigastric pain and tenderness to the extreme distention of the stomach.

Neither Dr. Bingham nor myself could detect either tenderness or rigidity over the region of the appendix a few hours before the symptoms of general peritonitis developed.

In appendicitis my own experience is that whereas pain may be referred to the epigastrium or other areas, yet tenderness on pressure and at least some rigidity over the region of the appendix, are almost invariably to be demonstrated by careful examination.

Unfortunately a postmortem examination was not permitted, but I[21] was of opinion that there was a generalized infection, with involvement of the lymphoid tissue, in both the stomach and appendix to account for the symptoms.

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[21] The above opinion was expressed seven years ago. Since this paper was read in July, 1914, Edward C. Rosenow has published his article on the Bacteriology of Appendicitis and its Production by Intravenous Injection of Streptococci and Colon Bacilli, Journal of Infectious Diseases, March, 1915, xvi, 240, in which he proves, experimentally, that such multiple hematogenous infection of the appendix, duodenum, small intestine, and stomach may occur.

Another possible explanation of the early gastric symptoms is that they were due to a generalization of the infection from the tonsil with secondary involvement of the appendix, or to an infection of the appendix by way of the alimentary tract; in either case the acute early process subsiding with coincident improvement for some days of the pulse, temperature, gastric condition, and general symptoms. After smouldering in the appendix the infection suddenly became active with the onset of fulminating symptoms.

In Dr. Main's case there was definite evidence of involvement of areas in the small and large intestine, as well as of the appendix, suggestive of a hematogenous infection. The evolution of symptoms would suggest that an infection from the tonsils of the lymphoid tissue in other areas of the alimentary tract had occurred, and after smouldering for a time suddenly became active with the onset of fulminating symptoms.

In this case it is interesting to note that the patient complained of slight pain and tenderness in the right iliac region, which, however, had disappeared by the next day (March 5). The acute fulminating symptoms appeared March 16 after the patient was apparently well, suggesting that in the interval the infection in the appendix had remained dormant.

Dr. Arthur Wright has furnished me with notes of the following case from Dr. G. A. Bingham's clinic in the Toronto General Hospital.

Mrs. W., aged forty-seven years, came under observation on April 1, 1914. She had for the previous three days been suffering from pain in the right lower abdomen, radiating to the back. She had previously suffered from acute rheumatism (more than thirty years ago), and two years previously had been treated in the Toronto General Hospital for cardiac trouble. There was profuse uterine discharge, in which gonococci could be demonstrated, and there was also retroversion of the uterus. A parovarian cyst was removed.

On June 10 the patient complained of a sore throat, and on June 12 the tonsils were found to be enlarged and reddened, and there was marked pain on swallowing. On June 16 there was abdominal pain of sudden onset, commencing in the umbilical region, and followed by vomiting. The pain gradually became localized over the region of the appendix, but the temperature and pulse remained normal.

On June 17 the symptoms had become more severe, and pain, tenderness, and rigidity of the right rectus were present to a marked degree, and there was a mass in the appendicular region. Evening temperature 103°; pulse, 114. Leukocytes 21,400. The tonsils were still inflamed.

An operation was performed at 8.30 P.M. and a gangrenous appendix, in a retrocecal position, was removed. Recovery occurred, and on June 26 the patient no longer complained of pain or soreness of the throat.

In conclusion, I[22] would like to emphasize the following points:

1. The importance of bearing in mind the liability of appendicitis to follow acute tonsillitis.
2. That the appendicular involvement may be only part of a generalized infection, hence the gravity of such cases out of proportion to the local symptoms.
3. The tendency for such cases to be atypical in their clinical course, and after smouldering, to suddenly develop fulminating symptoms.
4. Chronic tonsillar infections should be kept in view as the possible cause of similar infections of the appendix.
5. That whereas at least some degree of local tenderness and rigidity are almost always to be elicited on careful examination of the abdomen in the right iliac region in acute appendicitis, in rare cases these signs may be absent.

LIGATION OF THE PORTAL VEIN IN SUPPURATIVE PORTAL PHLEBITIS.

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The problem of attacking pylephlebitis along the lines employed in septicemia of otitic and of uterine origin, has as yet attracted no great attention.[1] A. G. Gerster,[2] commenting on this disease, says: "The evacuation of septic thrombi from the jugular vein in mastoid disease has yielded such excellent results that the application of the principle to the portal vein would be natural and logical. But the anatomical relations, while very favorable in the former instance, are just the reverse in the latter. Only a short piece of the portal vein, that situated in the hepatoduodenal ligament, is approachable. The two mesenteric veins and the splenic are practically inaccessible. Hence, though phlebotomy of the portal trunk in the hepatoduodenal ligament is not impossible, the evacuation of thrombi by flushing through a catheter seems to be too problematic, not to mention the technical difficulties the surgeon might encounter in the closure of the phlebotomy wound."

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[22] Read before the Canadian Medical Association, St. Johns, July, 1914.

[1] H. Kehr, Chirurgie d. Gallenwege, 1913. Suppurative thrombi in the portal vein have never been removed operatively. Such a procedure might possibly have a beneficial effect.

[2] Trans. Am. Surg. Assoc., 1903.

More recently, H. Neuhof,[3] in his work on the experimental ligation of the portal vein, has called attention to the following important facts: "Although the portal vein has been more or less completely ligated for accidental injury in a very few instances (possibly two cases), a deliberately planned ligation has never been practised." Further, "The fact that no surgery of the portal vein has as yet developed, appears to depend upon the results of animal experimental studies. Many observers have demonstrated that ligation of the portal vein regularly leads to death in a very short time—in half an hour to two hours."

On the other hand, by experimental work Neuhof has established that gradual occlusion of the portal vein is not fatal. The cases of Brewer and Burdenko[4] indicate that in human beings a gradual occlusion due to pressure, followed by a ligation, is compatible with life, provided collateral circulation has been established. In view of these facts, Neuhof advocated ligation of the portal vein in suppurative pylephlebitis, realizing that the portal thrombus by gradually occluding the portal vein might have induced the development of a collateral circulation prior to the ligation of the vein, and that such a ligation would prevent further bacteria being swept from the radicles of the superior mesenteric vein into the liver. In animal experiments, moreover (Burdenko), it has been shown that the portal vein may be ligated successfully, provided there are preformed anastomoses produced by operative adhesions between the parietes and the omentum and intestines.

Guided by such considerations, and having realized some years ago that an interference at a lower level (*e. g.*, ileocolic vein) would have no effect, the following case was operated upon. The plan of procedure, as soon as the diagnosis was made, was as follows: To insure an adequate collateral circulation, I wished to make, if possible, a venous lateral anastomosis between the left spermatic vein a few inches below its confluence with the left renal vein and one of the larger branches of the inferior mesenteric vein.[5] In this way, the portal and systemic circulations would be satisfactorily anastomosed. In addition, I proposed to perform an omentopexy to establish other anastomotic paths. At the second operation, I planned to ligate the portal vein, to cut the vein above the ligature and drain the hepatic end with rubber tube run into the lumen of the stump and at the same time perform a cholecystostomy to drain the biliary system.

All that I planned to do I was not able to carry out, as will be seen from a perusal of the case report. Owing to the interest of such a case the data will be given in some detail:

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[3] Surg., Gyn. and Obst., 1913.

[4] Deutsch. Ztschr. f. Chir., 1913, cxxiv.

[5] The application of this idea to the treatment of cirrhosis might prove of value.

Case Report.—H. G., aged twenty-five years; shipping clerk; married. Admitted February 20, 1915. Died March 1, 1915.

Diagnosis. Acute gangrenous appendicitis. Operation: Appendisectomy.

Postoperative Complications. Pylephlebitis. Secondary Operations: Omentopexy, ligation of portal vein. Cholecystostomy.

Family History. Father and mother dead; five brothers all well; two sisters also well. No tuberculosis or cancer in family.

Past History. Patient smokes ten cigarettes a day. Drinks occasionally. Had gonorrhea three years ago. Denies syphilis, pneumonia, scarlet fever, typhoid, etc. Two weeks ago had grippe and sore throat.

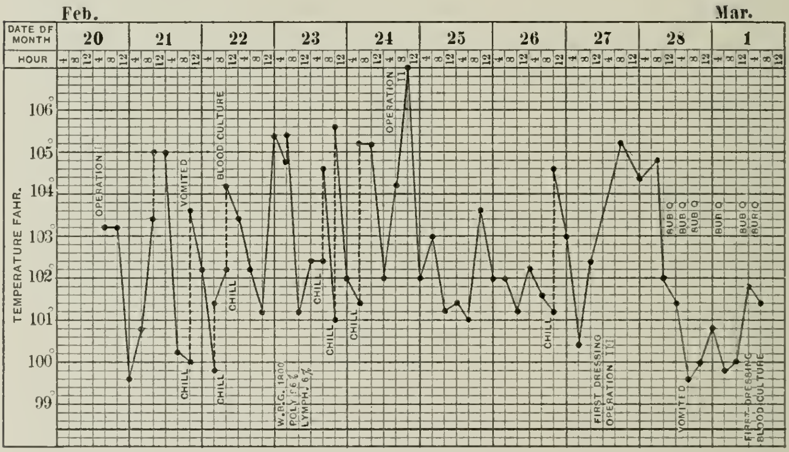

Fig. 1.—Temperature chart.

Present History. Wednesday, February 17, 1915; in the morning the patient experienced general abdominal cramps, associated with vomiting, constipation, chills, and fever. The general pains subsided and became localized in the right iliac region. Patient has been thirsty and has had frequency of urination. Since the day of onset, also very much prostrated, not having had any sleep on account of the pains. Has no cardiorespiratory or renal complaints.

Synopsis. Pain in right iliac region since Wednesday.

Physical Examination. *General Condition.* Good. Patient is well nourished.

Head. Eyes react to light and accommodation. No palsies; no petechiæ. Tongue coated. Teeth in good condition. Pharynx congested. Tonsils negative. Ears and mastoid and thyroid negative.

Glands. Negative. *Chest.* Expansion fair and equal. Lungs, anterior and posterior negative; no dulness, no rales. Heart, U. B., third rib; R. B., right border of sternum; L. B., fifth space midclavicular line; sounds booming at apex, slight roughness of the first sound; sounds negative at base.

Pulses. Equal, regular, and of good force; tension not increased but rapid.

Abdomen. Symmetrical; tympanitic; tenderness, rigidity, and spasm of right rectus muscle in the iliac region; rebound sign positive. Spleen, kidney, and liver not palpable.

Rectum. Tenderness and sense of resistance in the right iliac fossa.

Extremities. Negative.

Synopsis. Tenderness, rigidity, and spasm of right rectus muscle in right iliac region.

OPERATIVE PROCEDURES. *First Operation.* February 20, 1915. (Dr. Shlimbaum, house surgeon) G. and E. Appendicectomy for acute gangrenous appendicitis. Incision two and a half inches, right rectus muscle splitting.

Findings. Appendix found to be entirely gangrenous with fibrinous exudate on tip. No evidence of thrombosis in mesenteriolum.

Procedure. Amputated in usual fashion: stump carbolized, closure of abdominal wound in layers.

Specimen. Last inch of appendix somewhat bulbous, gangrenous and contains foul-smelling pus.

February 21. Looks very septic; two chills. Temperature, 99.8° to 105°; pulse, 106 to 132. Blood culture taken today showed streptococci. Has severe right-sided abdominal pains. Jaundice present.

February 23. Leukocytes, 18,000; polyneuclears, 94 per cent.; lymphocytes, 6 per cent.

February 23. Since operation the patient had chills daily and septic temperature. Conjunctivæ deeply icteric. Complains of pain in right hypochondrium, where there is distinct tenderness over liver, which is distinctly enlarged. Wound clean.

February 24. Jaundice more marked today. Chills and high temperature persist. Tenderness over liver more marked. *Diagnosis:* Suppurative portal phlebitis.

Second Operation, February 24. (Dr. Beer, G. and E.) Patient taken to operating-room with idea of anastomosing inferior mesenteric vein and spermatic (left), and doing an omentopexy so as to establish collateral circulation preliminary to ligation of portal vein for pyelophlebitis.

Incision along the crest of the ilium to left of left rectus muscle. Lower pole of kidney and ureter exposed. Spermatic vein isolated. Vein branch of inferior mesenteric isolated. Attempt at making anastomosis was unsuccessful, owing to very small caliber and thin wall of inferior mesenteric branch. Peritoneum was then opened to make an omentopexy and portal fissure palpated. Fair-sized indurated area and enlarged glands palpable at portal fissure. Omentum brought down and sutured to parietal peritoneum with plain catgut suture. Peritoneum then repaired as usual. Wound closed in layers.

NOTE. No ascites. Vessels in omentum and branches of inferior mesenteric vein showed little abnormal congestion.

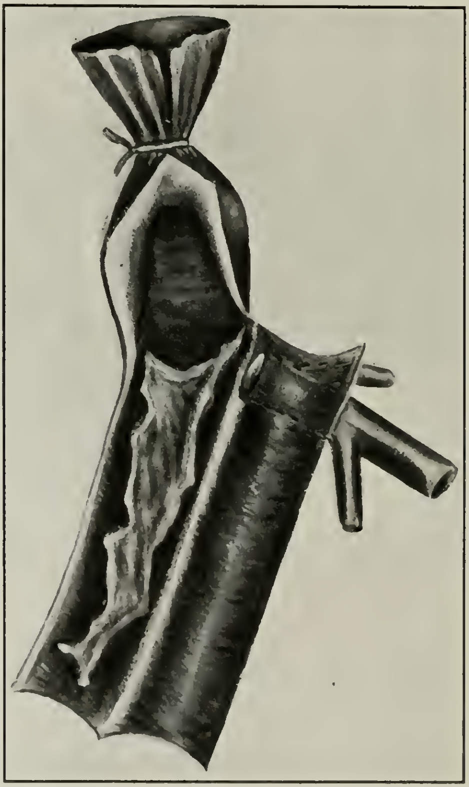

FIG. 2.—Sketch of ligated portal vein and branches with suppurating adherent thrombus proximal to ligature.

February 24 to 27. Patient seemed to remain about same. Temperature was lower and only one chill.

Third Operation. February 27. Ligation of the portal vein for suppurative phlebitis; cholecystostomy for drainage of the bile tract (Dr. Beer).

Incision four to five inches right rectus from ribs to level of umbilicus. Small amount of bile-stained fluid in the peritoneal cavity. Marked venous congestion of the stomach and gastrohepatic ligament. As the foramen of Winslow was shut off, and as the distended gall-bladder prevented an easy approach to the region of the portal vein from the right side, the peritoneum over the vein was opened just above the duodenum over what appeared to be the site of the portal vein. Numerous glands of deep red color blocked the approach, and dissection along the tract of the hepatic artery caused very disagreeable bleeding. The bleeding was controlled and a cholecystostomy performed. Then another attempt was made to reach the vein after exposing the choledochus for two inches. This approach was not blocked by glands and exudate, and the large blue vein was found mesial to the duct on a slightly deeper plane. It was impossible to state that there was a thrombus within, though the walls seemed thicker than normal. A ligature was thrown about the vein and, on pulling it sufficiently tight to occlude the lumen, no change in the patient's pulse was detected (Dr. Wilensky). Thereupon the vein was tied with heavy catgut. Rubber dam to ligature coming out along the gall-bladder tube. Wound closed and dressed.

Patient was much shocked and in poor condition when returned to ward at 5 P.M. Under heroic stimulation his condition improved.

February 27, 8.15 P.M. Condition fair. Pulse of fair tension. regular, and of rate of 140. Respiration regular and not rapid (34).

8.45 P.M. Condition unchanged. Tongue very dry, rough and brownish; fur on dorsum.

9.15 P.M. Salt solution not retained by bowel. Answers questions correctly.

9.45 P.M. Condition unchanged. Looks comfortable. Pulse and respiration unchanged. Mind perfectly clear.

10.45 P.M. Pulse 140. Good quality. Beats practically same in force, but occasionally one of weaker quality is felt. Was sleeping. Now awake. Recognizes surroundings and persons previously known to him. Jaundice apparently (artificial light) somewhat less marked. Tongue very dry in centre. Is taking fluids in two to three dram quantities without vomiting. Bile drainage, four ounces.

11.20 P.M. General condition pretty fair. Pulse 134, good quality, regular in rate and rhythm. Does not complain of any pain. Jaundice seems decidedly diminished, particularly of conjunctivæ. Breathing is regular, slightly increased in rate.

February 28 and March 1. Enemata effectual and flatus expelled. Edema of scrotum and lower abdominal wall (perhaps more on left side) present this morning; also of penis and suprapubic region. (Infection?) Retention of forty ounces of urine relieved by catheter.

Lumbar wound infected, fascial necrosis present. Sutures removed, wound opened widely and packed with iodoform gauze. Bile drainage six ounces.

Blood culture taken in morning showed Bacillus coli. In the afternoon patient became gradually comatose, and died forty-eight hours after operation without having given any evidence of blood either in vomitus or in stool.

Urine Report. February 21. Amber; acid; sp. gr., 1028; albumin, heavy trace; sugar and bile negative. Microscopically: hyaline casts, epithelial cells, and a few leukocytes.

February 22. Bile, negative.
February 24. Bile in urine.
February 25. Bile in urine.
February 28. Bile in urine.

Blood Report. February 25. Blood culture of 12 c.c., streptococcus.

March 3. Blood culture; Bacillus coli.

DIAGNOSIS. Acute suppurative pylephlebitis (secondary to acute gangrenous appendicitis). Ligature of portal vein. Streptococcemia.

INCOMPLETE AUTOPSY (by Dr. Baehr). *General.* Marked icterus, no petechiæ. Rigor mortis marked.

Abdomen. The abdominal viscera inspected through surgical incision along the right rectus muscle. No ascites. The portal vein found tied off with catgut about 1.5 cm. above the head of the pancreas. Distal from the ligature, the entire portal system was found to be filled with thick dark brown grumous purulent material consisting of pus mixed with some blood. In the portal vein near the bifurcation and in its left main branch, there were also flat purulent thrombi on the vessel wall. Proximal to the ligature, the splenic and inferior mesenteric vessels were found to be patent. The superior mesenteric and its right colic branch were found to be filled with yellowish white purulent material. In places there were also thrombi. The thrombosed vessels containing yellowish white pus led down to the region of the cecum and ileo-cecal junction. The vessels in the immediate neighborhood of the appendix site were empty and showed no suppurative process.

Gastro-intestinal Tract. Appears normal, showing no circulatory disturbance. The coronary veins along the upper half of the lesser curvature are widely dilated. The appendix stump appeared to be normal.

Retroperitoneal veins behind the ascending colon show a similar dilatation.

Liver. Slightly larger than normal. Its lower border reaches down about one finger breadth below the free border of the ribs. On section the organ is seen to be studded with areas in which there are numerous small yellowish foci consisting of collections of pus. In the immediate neighborhood of each of these areas is also a radicle of the portal vein, filled with dark grayish brown purulent material. The intervening liver parenchyma shows merely cloudy swelling. The common bile duct is patent and contains some thin yellowish bile.

Gall-bladder. Fastened to the abdominal wall by a catgut suture. A hole in its fundus is also closed with a suture. The organ itself contains a small amount of mucopurulent material which is slightly bile stained.

Spleen. About one-half larger than normally. No organs removed.

Bacterial Report. Bacillus coli from pus from liver.

MICROSCOPIC EXAMINATION. *Liver.* Capsule of normal thickness. There is moderate passive congestion in the centres of the lobules. The liver cells in this region are somewhat smaller than normal and contain granules of brownish pigment. In Glisson's capsule throughout the organ there are numerous and extensive round cell infiltrations. These have no relation to the bile ducts and the hepatic arteries. In some places, there are large collections of pus cells and cellular detritus, in the midst of which masses of bacteria are frequently to be seen. Most of these abscesses appear to extend from foci in Glisson's capsule. Many of the smaller radicles of the portal vein contain parietal blood-platelet thrombi. Their lumen usually contains red blood cells and only rarely collections of pus cells. The larger radicles of the portal vein appear to be for the most part completely destroyed by a suppurative process and in some places the abscesses can be seen to be extending from this by contiguity.

Spleen. Capsule and trabeculæ of normal thickness. Sinuses in the pulp and the large venus sinuses are markedly dilated. Malpighian bodies rather small, contain no germinal centres and are surrounded by a zone of congestion.

The most striking feature of this case of fulminating portal vein suppuration is to be found in the absence of all signs and symptoms of obstruction to the return flow of the portal blood despite ligation of the portal vein. How this is to be explained I admit I do not know. Whether it was accidental, and due to some anomaly in our patient's circulation, or whether the short duration of the incomplete portal obstruction had forced collateral circulation to such an extent, it is impossible to say at this time. That complete ligation of the portal vein did not lead to some engorgement of the viscera surprised me very much, as I do not believe that the omentopexy gave much assistance to the return flow. Unfortunately the patient's condition became so bad during the third operation that I was not able to do what I had planned, *i. e.*, cut across the portal vein above the ligature and drain the hepatic end with a tied-in tube. Knowing the remarkable power that the liver has shown in fighting infection, I believe that this assistance would be of great value. Further experience along these lines will demonstrate whether one can expect to save these cases in the manner outlined in this paper.

A REPORT OF THREE CASES RESEMBLING PSEUDOSCLEROSIS AND PROGRESSIVE LENTICULAR DEGENERATION.

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The disease known as pseudosclerosis was first recorded in 1883 by C. Westphal. This observer described two cases in which tremor was the most conspicuous symptom. In these cases the symptoms resembled those of disseminated sclerosis in some other respects, but when the brains of these two patients were examined after death, they did not present the usual appearance of the brain in disseminated sclerosis; in one of the cases, however, the brain did show a generalized increase in consistence, but in the other case nothing abnormal was discovered.

Although Westphal seemed fairly certain that the cases he observed were representative of a disease that had not up to that time been recognized, he found it difficult to define its boundaries sharply. The term pseudosclerosis was, therefore, apparently coined to designate the condition.

These observations remained for a long time unnoticed until Strümpell[1] carefully analyzed and described the symptomatology of his own and of Westphal's cases, with the result that he was able to distinguish clearly between, and to separate this condition from, multiple sclerosis.

Similar cases have been recorded by the late Professor Frankl-Hochwart,[2] of Vienna, and also by Fickler[3] and others, but little of importance had been published that could throw any light upon this subject until the observations of Völsch[4] appeared.

Völsch's patient was a girl, aged seventeen years, who had suffered for about two years from pronounced rhythmic tremors of the limbs and trunk and spastic contractures of the extremities, together with dysarthria and dysphagia, and who showed pigmentation of the cornea and of the skin. In this case the postmortem examination revealed marked atrophic cirrhosis of the liver, a condition that had not been diagnosed during life. No abnormality could be detected in the brain. This case was regarded by Völsch[5] as probably one of pseudosclerosis, of the type recognized by Westphal and Strümpell.

It was just at this time (September, 1911) that Wilson's very complete descriptions of the disease he termed "progressive lenticular degeneration" appeared.[6] In the appendix to that article Wilson refers to Völsch's case as probably one of lenticular degeneration, and, indeed, this opinion seems entirely justified, in spite of the fact that degeneration of the lenticular nucleus had not been discovered.

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[1] Deutsch. Ztschr. f. Nervenh., 1896, xii.

[2] Arb. aus dem Universität, 1903, Heft x, p. 1.

[3] Deutsch. med. Wchnschr., 1904, No. 51.

[4] Deutsch. Ztschr. f. Nervenh., 1911, xlii, 133.

[5] Ibid. 335.

Since then similar cases have been carefully studied and recorded: one by Hösslin and Alzheimer,[7] and one by Rumpell.[8]

In the cases that I am about to record here the condition resembled very closely the accepted disease-picture of pseudosclerosis.

HISTORY. The family consisted of two males and three females. Three of the members were affected and two were healthy. John and Annie were admitted to the wards of the Orthopædic Hospital and Infirmary for Nervous Diseases in Philadelphia, under the care of Dr. John K. Mitchell, during the winter of 1913, and at different times subsequently they have been under observation in the outpatient department. Thomas was never admitted to the wards of hospital, but has been under observation in the dispensary.

The patients stated that they came of healthy Irish stock, their parents having been people of good habits; that they themselves had not previously suffered from any disease, and that prior to the onset of their present malady, they had always been able to follow their occupations, John and Thomas as laborers and Annie as housemaid. Venereal disease was denied. John and Thomas admitted that they occasionally used alcohol to excess, but they did not appear to be alcoholic. Annie had always been a total abstainer. Thomas was married, his wife and two children being healthy.

CASE I.—John McC., aged forty-two years. The patient stated that when he was thirty-two years old he noticed "a shaking" of his right arm. He did not feel sick at that time, and declares that he had not been drinking. The shaking became gradually more pronounced, and he soon found that his legs were beginning to feel stiff and that his left hand also was "shaking." About six to ten months after the onset he was compelled to give up work on account of so much "shaking" and stiffness of his limbs; since then he thinks that the stiffness of his legs has gradually grown more and more marked.

Physical Examination.—The patient's expression is abnormal It differs from that seen in paralysis agitans in that it lacks the "fixed" look, and it varies also from the characteristic expression of Wilson's disease in that the spastic and contracted appearance of the facial muscles is lacking; there is, however, a decided tendency to widening of the palpebral fissures, lending to the face an expression that might be described as one of astonishment. This peculiarity seemed never to disappear entirely. There was no tremor of the lower jaw. The pupils reacted normally to light and in accommodation and in convergence; the ocular movements were well performed in all directions, and the ophthalmoscopical examination revealed nothing abnormal. Hearing also was normal.

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[6] Brain, 1911.

[7] Ztschr. f. d. ges. Neurol. u. Psychiat., 1912, Bd. viii.

[8] Deutsch. Ztschr. f. Nervenh., 1914, xlix, 54, 161.

There was a slight regular, continued tremulous movement of the head on the trunk, but there was no evidence of contracture of the muscles of the neck.

While in the standing position the patient presented a marked tremor of both upper extremities, the trunk, and the lower limbs. With the aid of a chair he could stand erect, but quickly became tired. The tremor of the upper extremities was somewhat more pronounced on the right side, and on both sides it was greater in the distal portions. It was a constant to-and-fro rhythmic flexor and extensor movement, which never ceased entirely, and it was always increased by emotion and by muscular effort. Moreover, any strong muscular effort of one extremity seemed to increase the tremor of the other limbs. In performing the finer movements with his hand there was a certain degree of awkwardness that appeared to be due more to increased muscle tone than to the tremor itself; still, spasticity was not very pronounced. The triceps and biceps tendon reflexes were equal and only slightly more marked than normally. Muscular power for all movements of the extremities was about the same on both sides, and was quite normal.

The abdominal and cremasteric reflexes were equal and normal.

His lower extremities were spastic and tremulous. Unlike the upper extremities, the tremor in the lower limbs was more marked in the thighs or proximal portions than in the distal parts. This was pronounced when the patient attempted to walk. Spasticity was fairly well marked, although he did not actually "stab" his toes on the floor when walking. There was no tendency to retropulsion or festination. The patient was able to walk short distances with the aid of a cane, but the effort caused a general increase of the tremulous movements throughout the body and extremities, and, as a consequence, he rapidly became exhausted. At times, because of spasm of the muscles, the right foot was strongly abducted and temporarily everted. The patellar tendon reflexes were distinctly increased, but equally so; the Achilles tendon reflexes also were exaggerated, but equal. Irritation of the soles of the feet caused a prompt flexor response of the toes.

Examination of the thorax and abdomen revealed nothing abnormal. There was no evidence of arteriosclerosis. The systolic blood-pressure was 140. The liver dulness was not diminished.

The Wassermann reaction with the blood serum was negative. The blood count was normal and the urinary examination was negative.

His mentality was, on the whole, good. He did, however, present a certain irritability and lack of initiative, and was somewhat dull; but whether or not his differed from the condition one frequently sees in patients suffering from severe chronic disease is questionable.

There was no discoloration of the skin on any part of the body, and pigmentation of the cornea was also absent.

Case II.—Annie McC., aged thirty-eight years. The patient stated that she had been healthy until she was thirty-four years old, at which time, she declared, she gradually became more and more "nervous" (she explained that she used the term "nervous," meaning tremulous), and that her limbs became so stiff that she had great difficulty in getting about. She also stated that in less than a year's time after the onset of the tremor she had to give up work. Although at the present time she is not entirely incapacitated, it is only with the greatest difficulty that she is able to go up and down stairs.

Physical Examination. The patient is of average height, but appears to be thin, weighing about one hundred pounds. Her generalized tremulousness is very striking. Her pupils are equal and react normally to light and in accommodation and in convergence. The ocular movements are normal in all directions, and the ophthalmoscopical examination revealed nothing abnormal. There is no pigmentation of the cornea. The cranial nerves all seem to functionate normally; but the facial muscles, particularly on the right side, show a distinct tendency toward spasticity. The widening of the palpebral fissures and the expression of astonishment seen in the other patient are lacking here; nevertheless, this patient's expression, while it does not seem to be entirely normal, is not, on the other hand, characteristic. There is a decided regular tremor of the lower jaw, which is constant, so that the act of puckering the lips is done with difficulty. Her speech is indistinct—not dysarthric, but merely the speech of tremor. Swallowing is performed without any difficulty. There is a slight yet distinct tremor of the head on the trunk, but there are no spasmodic contractures of the neck muscles.

The upper extremities show quite marked to-and-fro flexor and extensor movements, which are more pronounced in the distal portions and equal on the two sides. When the patient stands with the arms hanging at her side a distinct and regular tapping sound is made by her hands striking against her skirt. The arms are slightly spastic. The biceps and triceps reflexes are active and equal on the two sides, but are not increased.

The movements of the extremities in this case, although not greater than those shown in Case I, did present an element of incoördination that was lacking in the previous case, or, at least, was much less conspicuous. At times, when using her hands for the finer movements, the fifth finger and the fourth finger were held in partial flexion and partial abduction. This resembled, but was not identical with, an athetoid condition.

The muscles of her back are held somewhat rigidly, and there is a tendency for the trunk to be drawn to the right side, as if the deep muscles of the back were in the early stages of a permanent contracture.

The abdominal reflexes are equal, but are difficult to elicit.

The lower extremities are very tremulous and moderately spastic. The patient can walk about the house and go up and down stairs only with great difficulty, and with the assistance of bannisters and cane; she is frequently compelled to stop to "quiet down."

The tendon reflexes of the lower limbs are moderately increased, but equal. There is no Babinski sign, and ankle-clonus is absent. Sensation everywhere is normal. There is no discoloration of the skin. The abdominal and thoracic organs show no abnormalities. The liver dulness is not diminished. There is no evidence of arteriosclerosis. The systolic blood-pressure is 136 mm.

The Wassermann reaction in the blood serum is negative. The blood count is normal and the urinary examination is negative. Mentality is normal.

Case III.—Thomas McC., aged thirty-four years. The patient states that when he was thirty-two years old he first began to feel "shaky." This was at first noticeable only in his hands, but later, he states his legs also began to tremble. He thinks that the tremor is not increasing, but that his legs are getting stiffer.

Physical Examination. The patient appears well nourished and muscular. His pupils are equal and react normally, and his vision is also normal. The eye-grounds were not examined. All his cranial nerves act normally.

His articulation is clear and distinct, and he has no difficulty in swallowing. His expression is normal, and there is no tremor of the jaw or of the facial muscles.

The muscular power of the upper extremities is equal and normal, as are also the triceps and biceps tendon reflexes. There is a distinct regular tremor of both hands. The patient shows a tendency to hold both arms partially flexed at the elbow, and the tremor is not unlike that of paralysis agitans, but lacks the "pill-rolling" position of the fingers so common in the latter disease.

While the tremor does not disappear, it is not increased on voluntary movement. With the patient in the sitting position, scarcely any tremor of the low extremities and trunk is noticed; but when he stands erect a slight regular extensor and flexor movement is noticeable at the knees. While this is not marked, it is, nevertheless, perfectly distinct. The lower limbs are slightly spastic, but locomotion is not markedly impaired. The patellar tendon reflexes and the Achilles tendon reflexes are equal and slightly increased. There is no Babinski sign.

Although the patient's mentality may have been entirely normal, he found fault with physicians, was very irritable, sulky, and sullen, so that reëxaminations and laboratory examinations could not be completed.

Summary. These three patients were all very striking in appearance. They presented tremor of the upper extremities, which began gradually and increased in severity, spreading slowly throughout the body, and involving the lower extremities as well; at the same time a gradually increasing tonicity of the muscles developed, until finally all voluntary movements and locomotion were greatly affected.

Dysarthria was not well defined, but in one case articulation was indistinct. Characteristic mental disturbances were lacking in all.

The diagnosis of these cases, based on purely clinical observation, would seem to preclude the possibility of an existing multiple sclerosis, for the usual symptoms of that condition were lacking—there was no nystagmus, the eye-grounds were normal, and there were no disturbances of sensation. A certain amount of muscular weakness was evident, but it was not greater on one side than on the other, and it did not even approach true paralysis; yet increased muscular tonicity was very general.

The tremor was more violent and of greater amplitude in Cases I and II. It was of a to-and-fro or backward and forward movement, showing some increase on voluntary movement, but being entirely free from the uncertainty of direction that in so many cases of advanced multiple sclerosis exhibit on voluntary movement. The tremor in Case III was much milder, and more closely simulated the regular rhythmic movement of paralysis agitans.

The difference in symptoms presented by these cases to those of progressive lenticular degeneration was indeed indefinite, for the condition appears to have been a family affection, very slowly progressive in character, but not, however, developing, as did Wilson's, in youth. The tremor seems to have been almost identical in character, but the degree of spasticity was slighter, and contractures were not observed, nevertheless, a tendency to tonic muscular spasm was present in one (Case I).

Strümpell[9] has referred to certain similarities that pseudosclerosis bears to Wilson's disease, and points out that in characteristic cases of pseudosclerosis the tremor is more conspicuous than the spasticity; whereas in lenticular degeneration the spasticity and contracture are more marked than the tremor, for it is known that lesions of the lenticular nucleus are capable of producing high degrees of spasticity. Nevertheless, if spasticity and contracture of muscles were sufficiently great, tremor of that part must of necessity grow less pronounced, for the limb may become partially fixed. This did occur in one of my cases.[10]

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[9] Deutsch. Ztschr. f. Nervenh., 1913–1914, l, 455.

Without a postmortem examination it would seem uncertain whether a positive differential diagnosis would be entirely justified for the only sign that has not been described in literature as common to both these diseases seems to be the curious brownish discoloration of the skin and pigmentation of the cornea that were observed by Fleischer,[11] Völsch,[12] and Holloway.[13]

Stöcker[14] has recorded a case of progressive lenticular degeneration in which he found lesions in the lenticular nucleus which he believed to be characteristic of that condition, but, in addition, he found distinct alterations of the glia elements in all parts of the central nervous system except in the cerebellum, and he directs attention to the analogy that exists between progressive lenticular degeneration and the pseudosclerosis of Westphal and Strümpell.

On the other hand the cases of typical pseudosclerosis of Alzheimer and Hösslin[15] and A. Westphal[16] revealed not only the characteristic changes in the glia tissue in various parts of the brain, but these observers state that these alterations were most marked in the corpus striatum and the optic thalamus.

Considering both the clinical and the pathological evidence now at our disposal, even though this is somewhat limited, it would seem not at all unlikely that, in the near future, pseudosclerosis and progressive lenticular degeneration may be proved to be merely modifications of the one disease. At all events the cases of Stöcker, A. Westphal, and Hösslin and Alzheimer appear to justify the opinion that, on purely clinical grounds, a differentiation is not possible.

VALUE OF RECTAL FEEDING.[1]

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Everyone having experience with rectal feeding by the introduction of a pint or more of liquid nourishment at a time, is impressed with the discomfort and difficulties of continued nutrition by this means.

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[10] Jour. Amer. Med. Assn., January 31, 1915.

[11] Deutsch. Ztschr. f. Nervenh., 1912, xl, 3.

[12] Loc. cit.

[13] Amer. Jour. Med. Sci., 1914, cxlviii, 235.

[14] Ztschr. f. d. ges. Neurol. u. Psychiat., 1914, xxv, 217.

[15] Ibid., 1912, viii.

[16] Arch. f. Psychiat., 1913, li.

[1] Read at a meeting of the American Gastroenterological Association, May 15, 1915.

An examination of stools shows how little food is really absorbed. On this account, for the past four years, I have been using the drop method as first introduced by Murphy for saline solution.

Four to eight ounces of peptonized milk with one pint of 4 per cent. sugar solution has been given three times daily. This method can be kept up for two weeks without discomfort. In a few cases they have caused cramp-like pains for the first day or two. In one or two cases vomiting has been produced. In but one case has it been necessary to give up the rectal feeding.

That the nourishment is carried well up to the intestines is shown by our experience in a case of fecal fistula after an appendix operation.

The patient was unable to retain any food by mouth, and rectal drop feeding was attempted. The dressings became invariably soaked with the enema after a few hours, showing that the fluid had made its way without difficulty through the length of the colon.

With rectal enemas of bismuth suspension there is no difficulty in obtaining a complete picture of the colon, but bismuth never enters the ileum except in the unusual cases of patent ileocecal valve.

With the drop method the same results were observed; no bismuth passed into the ileum.

In order to obtain some idea of absorption of rectal feedings by the Murphy method, metabolism investigations were made on cases of gastric and duodenal ulcer with no abnormality of nutrition. After the second day of artificial feeding, with nothing by mouth, the colonic intakes for four to six days in nitrogen was compared with the output in the urine and the return loss per rectum. Daily total nitrogen estimations of the urine were made while all the matter passed per rectum in the same period was collected, dried to constant weight, and the total estimated by the Kjeldahl method.

Case I.

		Urine.		
Day.	Nitrogen intake.	Amount c.c.	Output T. N.	Stool.
3	1.95	11.25	11.82	0.78
4	1.95	7.00	9.79	0.78
5	1.95	13.80	11.72	0.78
6	1.95	10.10	12.19	0.78
7	1.95	16.00	12.12	0.78
	9.75		57.64	3.90
	Total output		3.90	
			61.50	
	Intake		9.75	
	Body loss in nitrogen		51.79	

Case II.—Gastric ulcer.

		Urine.		
Day.	Nitrogen intake.	Amount c.c.	Total nitrogen.	Amount from feeding.
3	1.95 gm.	10.75	12.82	1.39
4	1.95	9.05	12.01	1.39
5	1.95	8.00	11.15	1.39
6	1.95	8.25	10.20	1.39
7	1.95	8.50	9.63	1.39
	———	———	———	———
	9.75 total nitrogen		66.81 urine	6.95
			6.95 stool	
			———	
			72.76 total nitrogen lost	

Intake 9.75
Body loss in nitrogen . . . . . 63.01 in five days

Case III.—Gastric ulcer (?).

		Urine.		
Day.	Nitrogen intake.	Amount c.c.	Total nitrogen.	Amount from feeding.
3	1.95	9.80	10.09	0.91
4	1.95	8.40	9.42	0.91
5	1.95	9.20	9.61	0.91
6	1.95	8.70	8.72	0.91
	———	———	———	———
	8.80		37.84	3.64
			3.64	
			———	
			41.48	

Intake 8.80

Body loss in nitrogen . . . . . 32.68 in four days.

Case IV.—Duodenal ulcer.

		Urine.		
Day.	Nitrogen intake.	Amount c.c.	Total nitrogen.	Amount from feeding.
3	3.90	8.20	11.05	2.06
4	3.90	7.35	10.97	2.06
5	3.90	9.10	11.26	2.06
6	3.90	8.45	9.86	2.06
7	3.90	8.20	9.32	2.06
8	3.90	7.80	9.09	2.06
	———	———	———	———
	23.40		71.55	12.36
			12.36	
			———	
			83.91	

Intake 23.40

Body loss in nitrogen . . . . . 60.51 in six days.

Case V.—Duodenal ulcer.

		Urine.		
Day.	Nitrogen intake.	Amount c.c.	Total nitrogen.	Stools and amount from feeding.
3	2.92	8.80	11.56	2.19
4	2.92	7.50	9.80	2.19
5	2.92	7.60	10.68	2.19
6	2.92	8.60	10.39	2.19
7	2.92	7.60	9.28	2.19
	———	6.50	8.11	———
	14.50	———	———	10.95
			59.82	
			10.95	
			———	
			70.77	

Intake 14.50

Body loss . . 56.27 in five days.

The average loss of total nitrogen by urine and stool in these five cases was 12.9 gm. per day. The average loss in nitrogen from metabolized proteid as shown by the total nitrogen of urine was 11.7 gm. per day.

The largest amount of nitrogen we were able to supply daily by rectal feeding was 3.9 gm., of which 2.06 gm. were returned with stools. According to the observations of Fr. Müller, the stools of individuals taking absolutely no nourishment contains 0.2 gm. per day. With this deduction from our estimations of the return nitrogen we have in no case observed an absorption of more than 50 per cent. of the proteid supplied, and it has fallen as low as 30 per cent. The average amount of nitrogen absorbed in these cases was 1.14 gm. per day.

When we compare the amount of nitrogen lost by these cases with the amount it was possible for them to absorb by colonic feeding, we realize how little we accomplish.

The difference between nutritional enteroclysis and normal salt enteroclysis was a little over one-tenth of the tissue albumin loss per day.

Over the periods of time that rectal feeding is usually carried out it is from practical standpoints an almost negligible quantity.

INTRACRANIAL TELANGIECTASIS: SYMPTOMATOLOGY AND TREATMENT, WITH REPORT OF TWO CASES.[1]

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Operations for Jacksonian epilepsy have so frequently resulted in negative findings that I desire to call attention to a group of cases which yields to treatment. This group, though apparently not large, has, nevertheless, a characteristic pathological picture. I shall briefly consider this condition from three points of view: (1) symptomatology; (2) pathology; (3) treatment. This paper is based on two typical cases.

Case I (Private record).—R. D., a boy, aged ten years, whom I saw in 1909, had, three months after a fall, fever and convulsions confined to the left side of the body, which began in the leg. A complete left-sided paralysis developed, which cleared up in a month. Following this the patient was apparently well and bright at school during the next year; then he began to have monthly convulsions, beginning in the face, with marked irritability; occasional headaches and vomiting; he often started suddenly. Wassermann negative. The physical examination revealed a left knee-jerk more active than the right; a double Babinski and normal eye-grounds; color fields could not be taken on account of the youth of the patient. On opening the dura (Fig. 1) a huge bluish mass of vessels protruded, which were so dense in places that the underlying cortex could not be seen. This mass lay over the motor area. There were no branches connecting with the dural vessels. I considered it inadvisable to try to remove this mass. Following the operation the patient had acute suppression of urine for twenty-four hours, and then made an uneventful recovery. His condition remained unimproved. Therefore, at the family's urgent request, a month afterward I tried to remove this angiomatous mass, but the patient died twenty-four hours later. Autopsy showed grossly that the process was confined to the cortex. Unfortunately, no microscopic examination was made.

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[1] Read at the meeting of the American Neurological Association, New York May 6 to 8, 1915.

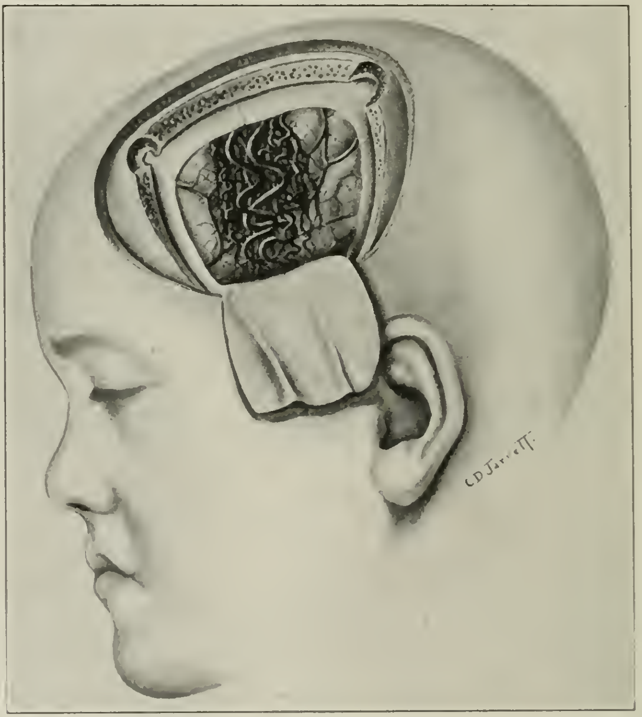

Fig. 1.—R. D., aged ten years. The very large size of the vessels of this telangiectasis is not sufficiently indicated on this drawing.

Case II.—C. E., a boy, aged ten years, surgical number 1873. Admitted February 8, 1915, discharged February 23, 1915. First seen in November, 1914. Referred by Dr. Schwab and Dr. Wolfner.

His past history was unimportant. First convulsion when three months old. There have been five since, three of these in the past three months. Unconsciousness lasted from one to two hours. All convulsions begin in the wrist of the left hand. There are minor attacks, occurring as often as five or six times a day. In these the patient seems sleepy and has a numb feeling in his hand. Wassermann negative. Physical examination showed a weakness of the two lower branches of the left seventh nerve on emotional exertion, and a pale telangiectasis over the forehead. The left eye-ground showed an old choroidal atrophy; the right eye was normal. Again, the color fields could not be satisfactorily taken on account of the youth of the patient. An exploratory craniotomy was performed in February, 1915. An angiomatous process was found in the dura, which on reflecting the dura was found to have numerous connections with the pial vessels (Figs. 2 and 3). This area of increased vascularity lay over the lower part of the motor area. All the vessels connecting with the pial vessels were ligated and the dural mass ligated above and below; then the dura was closed. Two days after

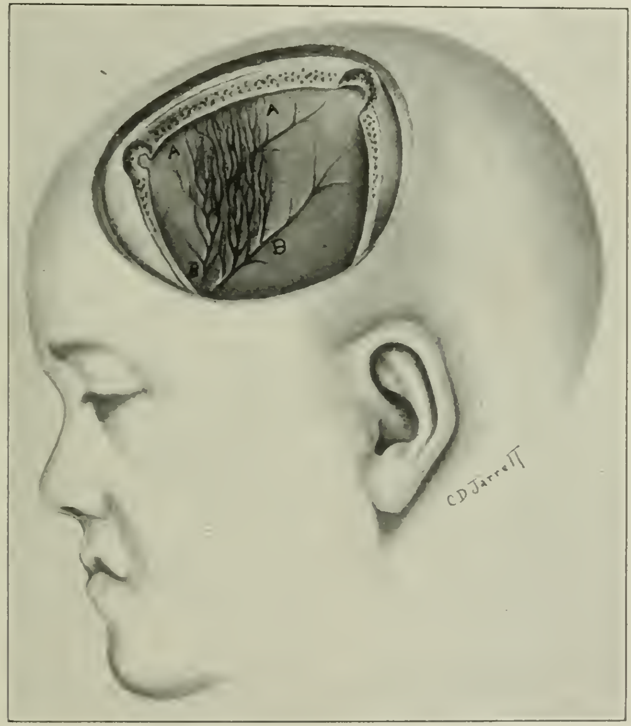

Fig. 2.—Case II.—C. E., aged ten years. Surgical No. 1873. Vessels were ligated at *A A* and *B B*.

the operation the patient had a violent convulsion. Since then he has been well. He has had three of the light attacks, of which he formerly had five to six daily. It is too early to express an opinion as to the ultimate result.

Both of these cases showed an unusual vascularity: the one of the vessels of the dura, which connected with the pial vessels, the other of the superficial vessels of the cortex.

In a careful survey of the literature I find that there really are very few cases like my second case. Virchow cites a case described by Hooper in his *Morbid Anatomy of the Human Brain*, published in 1828, which corresponds fairly closely. Pean gave a brief account before the French Academy of Medicine of an "angiome intracranien des meninges," which seems to have been identical.

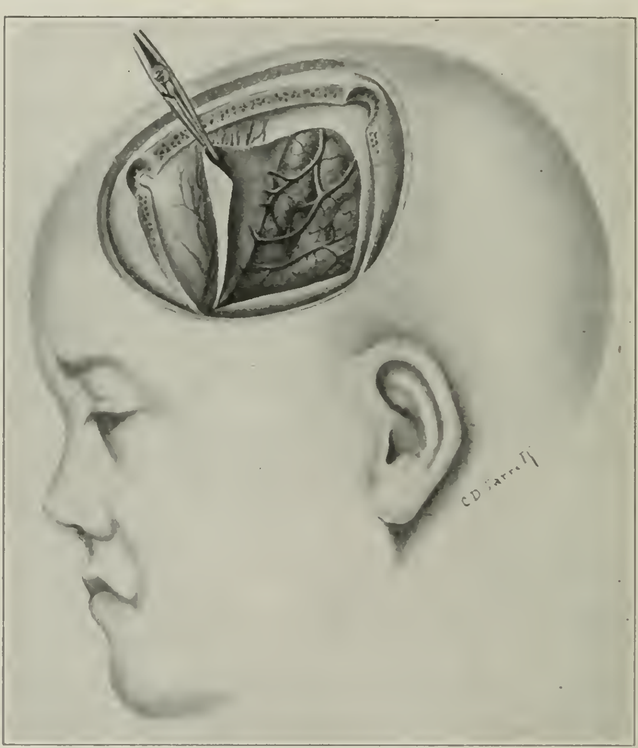

Fig. 3.—Case II.—The vessels shown running through the dura were all ligated.

Dr. Cushing, in 1906, described three cases of intracranial hemorrhage associated with trigeminal nevi. The process in all three of his cases was in the dura. He does not, however, mention the possibility that an identical process might occur on the cortex.

Oppenheim, in January, 1913, reported several similar cases in his paper on congenital brain tumors. He has given an admirable clinical picture of a condition which he calls angioma, which, in my opinion, is not an angioma at all but an entirely different pathological entity.

The first case is a type of which more have been observed. Krause in his book on the *Surgery of the Brain and Spinal Cord* reports two cases, one of which he has illustrated. This he calls an angioma venosum racemosum. In his opinion, evidently, he is dealing with a new growth—a true tumor. Tooth in his series of five hundred cases from the National Hospital has not a single instance of either condition. Bruns in his book on *Brain Tumors* makes the statement that cavernous angiomata and telangiectatic tumors have been found fairly frequently at operation,[2] and reports one case of what he calls an angioma which he observed himself. As he gives insufficient data it is impossible to decide to which of these two groups this case belonged. Virchow studied and described a number of such conditions, and was the first to clearly differentiate between telangiectases and true angiomata. He drew attention to the point which Adami emphasizes, namely, that a telangiectasis is a congenital dilatation of capillaries without any new-formed bloodvessels, while an angioma is a new growth and only properly so called when new bloodvessels are formed. In some of these cases the process is connected primarily with the capillaries, in some with the veins, and in others with the arteries. In true angiomata no vessels with all three coats developed are found, but in both of my cases the vessels looked prefectly normal, and were well formed.

In looking through the literature I find that these points are lost sight of and that the term angioma racemosum arteriale, or venosum, has been applied to conditions which were not actually new growths. I question very much whether Krause's case is correctly named. This, by the way, is the case cited by Oppenheim. It is the counterpart of my first case, and impresses me more like a telangiectatic process. Another point of interest is that cases like the two I have here reported are frequently, possibly always, associated with telangiectases elsewhere on the body, particularly on the face. My second case showed this. This was observed in Pean's case, also in Dr. Cushing's cases. Such cases as that of Emanuel, which he made the basis of an exhaustive discussion of angioma racemosus, are undoubtedly true new growths.

An etiological factor that has often been mentioned is trauma. Exactly what the relation of intracranial growths and trauma is, if any, is not at all clear. In certain cases it seems highly probable that a trauma has either irritated a preëxisting new growth, making it develop rapidly, or has actually been the cause of the new growth. In my first case there was a definite history of this sort, but the operative findings, it seems to me, exclude that factor, since there was no evidence of inflammatory reaction such as adhesions, connective-tissue overgrowth, or roughened inner layer of the dura overlying the dilated vessels.

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[2] At the meeting at which this paper was read, several members reported on published cases.

The classification of this process might seem merely of academic interest, but it has most important bearing on the treatment and prognosis. If this is a true new growth, extirpation is the procedure indicated, while if it is a telangiectasis, ligation should suffice. The question naturally arises, Will these thrombosed vessels, if left *in situ*, irritate the cortex, and should they therefore be removed after ligation? If possible the ligation should be planned so that the vessels do not remain filled with blood but are collapsed after the ligation. They will then atrophy and do no harm. This condition is a favorable one from an operative and prognostic stand-point.

It seems to me essential to distinguish more carefully between a true angioma—a neoplasm—and the process observed in these two cases, which is congenital and not a neoplasm. Undoubtedly some of the cases called angiomata have been misnamed. These cases, when reclassified, constitute a group which must be kept in mind in every case of Jacksonian epilepsy.

The clinical picture is quite a definite one.

1. Attacks of Jacksonian epilepsy occurring at long intervals in non-syphilitic young persons.
2. Unconsciousness of long duration.
3. No evidence of increased intracranial pressure.
4. A very slow progression of symptoms.
5. Telangiectases on the head or face.

For this condition I should like to suggest the name of intracranial telangiectasis.

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RESPIRATORY SIGNS AND SYMPTOMS IN TRICHINOSIS.

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One hundred and two case histories of trichinosis have been reviewed to determine the frequency of associated respiratory signs and symptoms which Dr. Edsall suggested may be more common than is generally realized, and which may be so well marked as to cause difficulties in the diagnosis, particularly in the early stage of the disease before the typical eosinophilia develops.

It should be noted that rales are often found in the lungs, usually at the bases, in a variety of acute infectious diseases, depending somewhat on the height of the fever and prostration, and in this trichinosis proves to be no exception.

In the literature there is reference to abnormal respiratory signs and symptoms in trichinosis. However, all the authors quoted, as well as others, in relatively long articles, refer to these respiratory signs and symptoms only in a casual way, devoting but a sentence or short paragraph to them, except as a late or terminal complication of the disease. No attention is called to the fact that respiratory complications may obscure the true diagnosis.

Staubli[1] states that very early there develops a bronchial catarrh. He explains that this is dependent upon the invasion by trichinellæ of the respiratory muscles, bringing about their insufficiency which leads to a scanty expectoration and ultimately to bronchopneumonic processes. Staubli remarks that the sudden rises of temperature with chills may be dependent on this.

Besides the mechanical involvement and irritation of the respiratory muscles by the embryos there is good evidence from the fact that the embryos occur in the blood stream and great veins (Staubli,[2] Herrick and Janeway,[3] Lamb,[4] Cross[5]) to show that they may be present in the lung tissue and cause irritation of the alveoli and bronchial mucosa directly.

Thompson,[6] in a report of 52 cases, says "cough may be present in a number of cases with a slight bronchitis, probably due to irritation of the bronchi by the parasites, but the latter were not found in any of the sputa examined."

Kratz[7] reported a total of 337 cases. Sixty-four of his 101 deaths were attributed to disturbances of the respiratory apparatus and 14 of these had hypostatic pneumonia. Rupprecht[8] also mentions pneumonia as a complication, especially in fatal cases.

Stiles[9] in his description says: "The respiration becomes difficult and respiratory troubles are likely to be severe, especially in the fourth and fifth week, and there may be severe dyspnea accompanied by violent asthma." Granger[10] also expresses the same view, though in his 18 cases reported no mention is made of any such respiratory signs or symptoms. Steiner[11] mentions involvement of the respiratory muscles by the parasites and the resulting paralysis as a cause of death.

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[1] J. F. Bergmann, Wiesbaden, 1909.

[2] Loc. cit.

[3] Arch. Int. Med., 1909, iii, 203.

[4] Amer. Jour. Med. Sci., 1910, cxlii, 395.

[5] Arch. Int. Med., 1910, vi, 301.

[6] Amer. Jour. Med. Sci., 1910, cxl, 157.

[7] Die Trichinenepidemie zu Hedersleben, Leipzig, 1886; Berl. klin. Wchnschr., 1865, lii, 509 (quoted by Staubli).

[8] Die Trichinenkrankheiten im Spiegel der Hettstädter Endemie betrachtet Hettstadt, 1864 (quoted by Staubli).

[9] Osler's Modern Medicine, 1907, i, 605.

[10] St. Paul Med. Jour., 1914, xvi, 399.

Mosler and Peiper[12] found bronchial catarrh only rarely. They do not mention pneumonia; while Leen[13] speaks of bronchial catarrh, which may at times amount to a bronchopneumonia or lobar pneumonia, but with no reference as to what stage of the disease this occurs or with what frequency.

Staubli says that at autopsy in a large majority of cases Cohnheim found a marked symmetrical bronchitis with frequent hypostatic conditions in one or both lungs but emphasizes that embolic processes are never seen. Frothingham[14] found hemorrhages into the lung tissue with embryos present, as did Askanazy,[15] who mentions embryos in the lung alveoli. They have never, however, been found in the sputum.

Romanovitch's[16] research has demonstrated anew that the trichina sows microbes along its path as it passes from the intestinal mucosa to the thoracic duct, great veins, and general circulation, and hence that the dominant character of the infection due to trichinæ is polymicrobian. He quotes Friedrich, who reports finding subcutaneous abscesses containing the trichinella, and he himself obtained positive cultures in 13 out of 23 rats killed at various intervals after infection with trichinæ and in 7 out of 10 guinea-pigs. He therefore concludes that fever, abscesses, and the fatal septicemia observed in man are due to microbes inoculated by the trichinæ. This offers an explanation of why lung infections may be common to this disease.

The 102 cases of trichinosis that are reviewed here have been taken from the records of the Massachusetts General Hospital (1899 to 1914), the Presbyterian Hospital in New York (1906 to 1914), and the Johns Hopkins Hospital (1899 to 1914).

The diagnosis in 70 per cent. of these cases was made by finding the embryo in excised pieces of muscle or in the blood; in 5 per cent. no parasite was found, but the muscle showed a histological picture of a myositis such as is found when trichinæ are present; in 25 per cent. by the history, symptoms, and physical signs, and the eosinophilia which varied from 13 to 63 per cent. of the total leukocyte count.

Those cases in which the final diagnosis of trichinosis was in doubt or in which a chronic cardiac or pulmonary condition existed have been excluded. One case that died was excluded because of an incomplete record. All of the 102 cases recovered except one, and it should be noted that although this patient had moderate dyspnea, no abnormal physical signs in the lungs were detected.

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[11] Boston Med. and Surg. Jour., 1908, cli, 721.

[12] Tiersche Parasiten in Nothnagel's spez. Patholog. u. Therap., 1894, vol. vi (quoted by Staubli).

[13] Boston Med. and Surg. Jour., 1913, clxviii, 601.

[14] Jour. Med. Research, 1906, xv, 487.

[15] Virchows Arch., 1895, cxli, 42 (quoted by Staubli).

[16] Comp.-rend. Soc. de biol., 1911, lxx, 257 and 339.

Five of these cases are of particular interest, because of respiratory complications, and are described in some detail later, leaving 97 cases which are here summarized; 8.8 per cent. of the total 102 cases (4 of the 5 cases described later and 5 of the 97 cases summarized) showed respiratory signs and symptoms severe enough to lead to the serious consideration or actual diagnosis of a purely pulmonary condition in the preliminary diagnosis.

Thoracic pain, usually in the region of the diaphragm or along the lower intercostal muscles, was not an uncommon symptom, but bore no relation to the presence of a slight or severe bronchitis, though usually when present was associated with a mild dyspnea and often with a shallow type of respiration.

The rate of respiration was usually increased with the fever to 25 to 32 per minute, reaching as high as 46, again varying with no regularity in regard to physical signs in the lungs except for the fact that those cases where the bronchitis was most marked usually had a higher rate than the others.

Of the 97 cases, 51 (50 per cent. of the total 102 cases) had no cough, nor was there any abnormality of the lungs noted in the physical examination during the first few days in the hospital or subsequently. The 46 remaining cases may be divided into three groups as follows:

I. Fifteen cases (15.3 per cent. of the 97) had cough without abnormal pulmonary physical signs, and only 3 of these raised any sputum.

II. Thirteen cases (13.6 per cent.) had not only a cough, but also abnormal physical signs were present in the lungs, though only 7 of them raised sputum. Thus 28 cases or 29 per cent. had a cough which began one to twelve days, usually about two to six days, after the earliest symptom of the disease, lasting three to twenty-five days, or through the course of the illness.

III. Eighteen cases (18.5 per cent.) had pathological physical signs of the lungs without there being reference to cough in the records.

Thirty-one cases, or 31.9 per cent. of the 97 cases (all the cases of groups II and III), showed abnormal physical signs in the lungs, which may be described as "very slight," "definite," or "well marked," according to the number of rales present.

(*a*) Very slight signs were noted in 11 cases, and consisted in 4 cases of rare dry rales, which are described in 2 cases as being scattered and in the other 2 as being at the bases. In 7 cases they consisted of a "few moist rales." In 3 of the 7 they were scattered, and in 4 were at the angles of the scapulæ.

(*b*) Definite signs, that is, distinctly more numerous rales, were found in 10 cases. In 1 they were "scattered subcrepitant" and in the 9 others moist (fine, medium, or coarse), located at the base in 4, the right axilla in 1, both apices in 1, the angles of the scapulæ in 1, and scattered in 2.

(*c*) Well-marked signs (rales very plentiful) were noted in 10 cases. In 2 of these the rales were of a dry type, in 1 at the bases only, and in the other "scattered all over." In the other 8 cases the rales were moist and of all varieties. In 5 of these they were everywhere in the lungs. In 2 at both bases, and in 1 at the left base only.

Ten of these 31 cases which had rales showed additional abnormal physical signs as follows:

Four had slight dulness with diminished respiration when the rales were at the bases.

At the point where the rales were most numerous, 2 showed slightly harsher breathing than normal, while 3 were noted to have suppression of breath sounds.

One case with rales at the left base showed dulness in this region and in the left axilla, where the breathing was distinctly diminished, but Roentgen-ray examination revealed only "peribronchial thickening."

The physical signs were first noted within forty-eight hours after the patient entered the hospital in 29 cases, while in the 2 others they developed within six days after admission, about eight days after the onset of the disease.

It has been difficult to tell from the records the exact duration of the abnormal signs in the lungs, though as long as the temperature remained elevated the signs persisted. However, it seems that as the temperature fell the signs began to be less and disappeared when it became normal, though in a few cases lasting some days longer. In the cases with the mildest signs they occurred only at the height of the fever and disappeared several days before the temperature was normal.

There was reference to sputum in 13 cases of the 102. No mention was made in the record of cough or sputum in one of these cases, yet a laboratory examination of sputum was noted.

In 7 cases the macroscopic examination of the sputum alone was noted; 3 were blood-tinged, of mucopurulent nature; 2 were "grayish white," while 2 were "mucopurulent."

Microscopic examination was made of 6 sputa, 4 of which grossly were "mucopurulent." At one time one of these showed blood streaks and 2 were "white mucoid."

Smears showed no tubercle bacilli in any of the sputa; many influenza bacilli were seen in 1 besides other organisms; 4 others showed a mixed growth of bacteria. The case which showed at first blood streaks in a mucopurulent sputum and later was only mucopurulent, contained many influenza bacilli. No eosinophile cells, Charcot-Leyden crystals, or parasites were discovered.

The following 5 cases, not included in the 97 cases referred to above, serve to show how pulmonary complications may obscure the diagnosis of trichinosis.

Case I.—This illustrates how a bronchitis or mild bronchopneumonia may be a prominent feature from the onset of the disease associated with a delayed eosinophilia.

Male, negro, aged thirty-four years, works in tunnels and is subject to decompression and compression for five minutes many times a day. *Family history, past history,* and *habits,* unimportant.

Present Illness. For three weeks he has had a cough, increasing in intensity, raising yellowish-white sputum which in the past two days has contained a little blood. During this time he has had a persistent soreness and tenderness of his legs, though not of a severe nature. Night sweats have been frequent.

For two weeks he has had a severe temporal headache, and has felt feverish, and during the past week his eyelids have been a little puffy in the morning.

Physical Examination. A well-developed negro, looking sick and coughing, having moderate tenderness of the leg muscles.

Nodes. Generally palpable. Rest of examination negative except for heart and lungs.

Heart. Normal size; sounds regular; harsh, short, systolic murmur is heard at the right second interspace, transmitted to clavicular region but not to neck. Second sounds are normal.

Lungs. Over both bases and in both axillæ, extending higher on left, are heard many fine, medium, and coarse moist rales. At a point half-way between the base of the left lung and angle of the scapula is an area of dulness where there is distant breathing of higher pitch than normal, with slightly prolonged expiration associated with a distant bronchial whispered voice.

Day in hospital.	Temperature.	Pulse average.	Respiration.
1st to 6th . . .	101.0° to 104.0°	100	30 to 25
6th to 16th . . .	98.0° to 100.0°	80	25 to 20
16th to 21st . . .	98.6° to 101.0°	85	25 to 20
21st to 33d . . .	98.0° to 99.5°	75	20

Blood: Hemaglobin, 90 per cent.

Day in hospital.	White count.	Polynuclear neutrophiles and transitionals.	Lymphocytes.	Eosinophiles.	Mast cells.
1st . .	10,500	86 per cent.	12 per cent.	2 per cent.	0 per cent.
5th . .	. . .	88 "	10 "	4 "	0 "
10th . .	9,300	80 "	8 "	10 "	2 "
17th .	. . .	69 "	13 "	18 "	0 "
27th . .	. . .	60 "	25 "	15 "	0 "

Trichinæ were found in a piece of gastrocnemius muscle on the sixth day after admission.

Sputum. On entrance this was "frothy-mucoid," with some purulent particles mixed with blood. A few influenza bacilli were present, otherwise negative. On the third to sixth day in the hospital, several examinations showed a mucopurulent sputum with many influenza bacilli. On the nineteenth day in the hospital a thick mucopurulent sputum was expectorated.

The signs present in the lungs persisted for five days, then gradually disappeared by the twelfth day. On the sixteenth day after entrance the moist rales reappeared, and on the twentieth day the area of dulness at the left base with harsh inspiration and expiration reappeared. A Roentgen-ray taken on the twenty-second day showed "the heart slightly enlarged to the right; question of dilated aortic arch. No tuberculosis." After this the lungs cleared and were quite free of rales on the twenty-ninth day.

Case II.—This case, though exhibiting no signs in the lungs, had an onset of a respiratory nature which caused the physicians to believe for some days they were dealing with a purely thoracic disease.

Male, white, aged twenty-six years; occupation, clerk.

Family history and *habits* unimportant.

Past history negative except for pneumonia three years ago.

Present Illness. Nine days ago he began to have a severe "cold," feeling very chilly, mean and weak since then. He has had a cough associated with slight pain in the front of the thorax, raising very little sputum; constant throbbing headache, aggravated by cough, has been persistent. There were no other symptoms.

Physical Examination. Negative throughout, except for neglected teeth with sordes and a few herpetic lesions on the lips. Temperature varied from 102° to 103°, gradually reaching normal on the eighteenth day after admission. The respiration was 25 to 30 per minute on the day of entrance. The day after 32 to 35, falling to 24 to 22 on the eighth day, and then averaging 20. The pulse during the fever was 100 to 90.

White count on entrance 11,800. (No differential count was made.)

Three days after entrance a few more herpetic vesicles developed on the lips. The record states the lungs were still negative, and the patient continues to cough a little. On this day a blood smear showed 7 per cent. eosinophiles.

Four days after entrance tenderness of the calves of the legs with pains "all over" developed.

On the eighth day marked muscle symptoms were present and a piece of excised muscle revealed trichinæ.

On the ninth day cough was still present, but with very little sputum. The symptoms gradually disappeared as the temperature dropped, the cough going by the eighteenth day in the hospital, when the temperature reached normal.

Case III.—The following case illustrates an onset with respiratory symptoms. A latent tuberculosis, possibly lighted up by the trichinosis, cannot be ruled out. It does not seem as if all the physical signs in the lungs and the respiratory symptoms could have been due to a previously quiescent tuberculosis, but that the trichinosis, which had existed for some time, was associated with a bronchitis.

Girl, aged thirteen years.

Family history and *past history* negative.

Present Illness. Three weeks ago she "caught cold" and had a chill that night; since then she has coughed a good deal, raising small amounts of yellowish-white sputum; breathing at times has lately caused slight pains in her chest. She has felt feverish, had severe headache, and sweats frequently at night. Pains in the legs and thighs have occurred, but were not severe.

Physical Examination. Very slight puffiness of eyes and tenderness on pressure of calves of legs and lower ribs was noted on examination, which was otherwise negative except for the lungs.

Lungs. Percussion showed the note in the left infraclavicular region slightly higher pitched than on the right. In the back a doubtful slight impairment in resonance at the left apex and at both bases. Breath sounds over upper left front rougher than normal, with expiration prolonged. Fremitus normal. Over both backs were numerous fine moist rales and at the bases sonorous rales; a question of an occasional dry crackling rale at the left infraclavicular region was noted.

Day in hospital.	Temperature.	Pulse average.	Respiration.
1st to 5th . .	101.0° to 99.5°	100	20 to 24
5th to 10th . .	98.0° to 99.0°	80 to 70	20
10th to 30th . .	96.5° to 97.8°	80 to 60	20

Blood.	White count.	Eosinophiles.
On entrance	24,840	53 per cent.
Twenty-seven days later	17,120	56 "

Calmette tuberculin conjunctival test, 1 per cent. negative; Calmette tuberculin conjunctival test, 5 per cent. positive.

Stools, urine, and blood culture negative.

A very small piece of muscle excised two days after entrance showed "no trichinæ."

The moist rales in the lungs were not heard after a few days, nor were the dry ones noted after the first examination. The slight dulness below the left clavicle with roughened breath sounds persisted. Neither cough nor sputum was mentioned in the record after the first three days in the ward. The tenderness of the calves of the legs and lower ribs persisted for the first week, and was not severe.

Case IV.—The case illustrates a sudden onset resembling pneumonia.

Male, aged twenty-three years, clerk in a grocery store.

Family history, past history, and *habits* unimportant.

Present Illness. Twenty-four hours before admission he was seized with a sharp pain in the left side of his chest, increased by breathing and coughing. The pain shifted to the right axilla and became more severe during the night. There has been some cough without expectoration. He had a chill this morning and one just after admission. He has felt feverish and prostrated since the onset.

Physical Examination. A well-developed and nourished man, appearing acutely ill, lying quietly in bed. Temperature, 103; pulse, 108; respirations, 30. The examination was negative except for much mucus in the throat, and the lungs showed some dulness in the right upper axilla, with slight whiffy bronchial expiration, but nothing definite.

Day in hospital.	Temperature.	Pulse.	Respiration.
1st to 6th . .	104.0° to 100.0°	110 to 78	30 to 20
6th to 12th . .	101.0° to 99.0°	100 to 75	24 to 20
12th to 17th . .	98.2° to 99.2°	88 to 74	24 to 20

The Roentgen-ray, upon the day of entrance showed "throughout greater portion of right lung shadow there is slight increase in density, and there are patches which strongly suggest early tuberculosis—slight irregularity in diaphragm shadow."

Five days after entrance all tendon reflexes were absent except the right knee-jerk and both triceps, which gave but a feeble response; and the note reads, "The signs in the lungs become no clearer; dulness on right side slight, but persists; breathing thought to be increased in apex of right axilla and interscapular region." The patient was quite cyanotic at this time. The record makes no further mention of the lungs or gives clinical notes of importance. No rales were ever present. The patient was discharged "well" sixteen days after entrance.

	Blood, white count.	Polynuclear neutrophiles.	Lymphocytes.	Eosinophiles.	Mast cells.
On admission . .	11,000	67 per cent.	23 per cent.	8 per cent.	2 per cent.
Six days later		72 "	19 "	9 "	0 "

Reds, 4,950,000; hemoglobin, 90 per cent.

The urine, stool, Wassermann, von Pirquet, and blood cultures were all negative.

Muscle excised nine days after entrance showed a distinct myositis with wandering cells and eosinophiles, and the muscle fibers show various stages of degeneration. Diagnosis: "myositis due to trichinæ."

Case V.—This case resembles pneumonia.' Unfortunately satisfactory history was not obtained, owing to his nationality; and a specimen of muscle was unobtainable. The diagnosis here is based on the eosinophilia.

Male, aged forty-four years, Italian laborer.

Family and *past history* unrecorded.

Present Illness. For two weeks he has felt sick and had a bad cough. During the past week he has been in bed with increasingly severe cough, chilly sensations, constant headache, and pains all over his body, especially in his legs.

Physical Examination. Well-developed man looking acutely ill and anxious, breathing rapidly, forty to the minute. The examination was entirely negative except for pyorrhea, sordes of teeth, and a heavily coated tongue. The temperature ran irregularly 101° to 103° in the morning, falling to 100° to 99° in the afternoon for the first ten days after admission, gradually declining after the first eight days. The following eleven days the temperature was normal. The pulse averaged 82 during the pyrexia and 74 when the temperature was normal. The respirations ran from 28 to 34 in the morning during the first eight days, except that in the first two days they were 44; in the evening they ran from 22 to 18 (perhaps due to morphin). With the descent of the temperature the respiration returned to normal.

Three days after admission a few moist rales without other signs were noted in the lower right axilla at the bases. The spleen was just palpable, otherwise examination remained negative. Nine days after admission a note states that "the patient continues to have a hacking cough, raising a little yellowish material." The lungs showed some scattered rales at the bases, present the next day also, though it is not stated when they cleared.

The patient was discharged twenty-two days after admission, having shown no abnormal symptoms or signs after the sixteenth day. No reference is found in the record of positive or negative evidence of muscle tenderness or other symptoms of trichinosis.

Day in hospital.	Blood, white count.	Polynuclear neutrophiles and transitionals.	Lymphocytes and large mononuclears.	Eosinophiles.
2nd	25,600	91 per cent.	9.0 per cent.	0.0 per cent.
10th . .	26,600	22 "	9.5 "	68.5 "
12th	27,000	26 "	11.0 "	63.0 "

Blood cultures, Widals for the typhoid group, sputum, urine, and feces were all negative.

From the above group summaries of the histories and physical signs in these cases it may not appear evident that there was sufficient reason for being misled at first as to the diagnosis. It is evident, however, from the complete records that such was the case. In the two cases that we personally had the opportunity to see and in another in regard to which we talked with the physician in charge, such certainly was the case, the pulmonary symptoms entirely obscuring the more ordinary ones of trichinosis for a time. It is quite probable that but for the hospital routine blood examination the proper diagnosis would never have been reached in some of the cases.

In Case I, which was seen by both of us, though the record states that the patient had muscle tenderness, it was not at all prominent when compared to the picture of an evidently sick man persistently coughing and whose lungs were filled with rales. Later when 4 per cent. of eosinophiles were found the muscle tenderness was given more consideration, which led to the finding of trichinæ in the excised muscle. For the first few days certainly the lung symptoms obscured everything else.

Case II had a history not unlike pneumonia: the patient looked sick, had a high temperature, rapid respiration, and labial herpes. It was not until the eosinophilia and muscle symptoms developed that trichinosis was considered.

In Case III trichinosis was made the probable diagnosis at entrance, owing to the high percentage of eosinophiles; yet the history given by the patient and her family was of purely respiratory character, and she exhibited well-marked signs of a bronchitis. The pains in the legs and edema of the eyes were both slight and noted only after finding the eosinophilia.

Those who saw Case IV felt at first they were dealing with a pneumonia, owing to the acute onset of symptoms of respiratory nature, with fever and signs in the lungs. Trichinosis did not occur to them until the second differential count of the white cells was made. The pulmonary signs might be explained by an old tuberculosis.

Again, Case V resembled pneumonia. The history was purely respiratory, the respiration high, and rales were present in the lungs. Trichinosis was not considered until the high eosinophilia was found on the tenth day after entrance.

Conclusions. In the literature, abnormal respiratory signs and symptoms in trichinosis have been noted, but without emphasis on the fact that they may obscure the diagnosis, especially when the patient is first seen. Bronchitis, bronchopneumonia, and lobar pneumonia have been spoken of, especially as a terminal event and chiefly in the earlier reported cases in Germany.

In 50 per cent. of the 102 cases studied there is no mention of cough or abnormal lung signs at any time during the course of the disease, but in the remaining 50 per cent., 16 cases (15.6 per cent.),[17] had cough without abnormal physical signs in the lungs, while 17 (16.6 per cent.) had cough with abnormal lung signs, making 33 cases (32.3 per cent.) that had cough beginning one to twelve days (usually two to six) after the onset of the disease and lasting three to twenty-five days or throughout the course of the illness; 18 cases (17.6 per cent.) had abnormal signs in the lungs but without cough, making 35 cases (34.5 per cent.) that had abnormal physical signs in the lungs. These physical signs were present within forty-eight hours after the patient entered the hospital in 32 cases (31.5 per cent.), and in 3 cases (2.9 per cent.) within six days. The duration of these signs seemed to depend on the length of time the temperature remained elevated, the signs disappearing as the temperature fell. If the signs were slight, they existed, as a rule, but for a few days, and only at the height of the fever.

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[17] This and the percentages given below are percentages of the total 102 cases.

Nine cases (8.8 per cent.) showed respiratory signs or symptoms, or both, severe enough to lead to a serious consideration or actual diagnosis of a purely pulmonary condition during the first few days the patients were in the hospital.

This percentage of cases leading to error in the diagnosis is greater than is usually recognized.

We acknowledge our indebtedness to Dr. Janeway, Dr. Longcope, and Dr. Edsall for permission to use their hospital records.

A TEST OF MYOCARDIAL EFFICIENCY, WITH REVIEW OF ONE HUNDRED AND TWENTY-SEVEN CASES.

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Some two or three years ago my attention was called to the fact that variation in systolic blood-pressure in relation to posture and exercise might be interpreted in terms of myocardial efficiency. Since then I have used a certain uniform method in a sufficient number of cases to warrant a review. Not all cases were studied in this manner, nor were any studied with the intention of tabulation. From the beginning the method has grown in favor, and I have come to look upon the blood-pressure picture—that is, the relation to each other of pulse, systolic, diastolic, and pulse pressure taken with the patient reclining and fully relaxed and again standing after light exercise—as a fair indication of myocardial efficiency. In these determinations I uniformly take the pulse, systolic blood-pressure, and diastolic blood-pressure with the patient reclining and fully relaxed; then I have him walk at his ordinary speed four times the length of my office, about 75 feet, and repeat the test in the standing position. This exertion is not sufficient to cause such subjective symptoms as dyspnea, palpitation, or chest pain unless the heart muscle be much impaired. It should not do this. It is a postural test plus sufficient exertion only to mildly stimulate the cardiovascular system.

I have tabulated all cases recorded, grouping them according to myocardial efficiency. It is obvious that a grouping on a basis of myocardial efficiency is open to error, and at the best can only be relative. I believe, however, that the lines of classification are sufficiently definite for the purpose.

Four groups are employed, namely, "good," "fair," "poor," and "bad." In group "good" are only normal or functionally normal hearts. In group "bad" are only those with broken (lost) compensation. It so happens that in the classification none appear in this group for the reason that the test was applied only to walking cases. The intermediate groups, "fair" and "poor," are not easily defined. In general, however, the cases in "fair" displayed mild subjective symptoms, while in "poor" the subjective symptoms were pronounced. I have subdivided group "fair" into "fair," "fair plus," and "fair minus" for reasons which appear in the text. In tabulating, in order to avoid the easy pitfall of making the case fit the conclusion, I first grouped the case and then noted the pulse, systolic and diastolic pressure and the pulse pressure reclining, and standing after light exercise. The grouping was governed by the subjective symptoms and physical signs as recorded and by my personal knowledge of the cases. The cases being selected from the heart clinic of a sanitarium, naturally the largest number fall in group "fair," for the reason that in such a clinic, walking cases predominate.

In Table I, not published, I have grouped the cases according to myocardial efficiency, that is, "good," "fair," or "poor," and have recorded pulse, systolic pressure, diastolic pressure, and pulse pressure, patient reclining and fully relaxed, and again standing after light exercise, together with the change in systolic pressure and pulse pressure, and the diagnosis.

TABLE II.

Group.	Whole number.	Increased or stationary S. B. P.	Per cent.	Decreased systolic blood-pressure.	Per cent.	Increased pulse pressure.	Per cent.	Stationary pulse pressure.	Per cent.	Decreased pulse pressure.	Per cent.
"Good"	13	13	100	0	0	11	85	2	15	0	0
"Fair" . .	85	55	65	30	35	35	41	24	28	26	31
"Poor"	29	12	41	17	59	6	21	6	21	17	58
Subgroup.											
Fair + ...	17	..	77	..	23	..	53	..	29	..	18
Fair − . . .	11	..	9	..	91	..	18	..	36	..	45

Table II is a summary giving under each myocardial efficiency group the whole number of cases appearing in that group, the number with increased or stationary systolic pressure, the number with decreased systolic pressure, and the number with increased stationary or decreased pulse pressure, each being noted also in terms of percentage. Table II best shows the contrasts and is the easiest comprehended if we read alone the percentage columns. For instance, in group "good" there are thirteen cases. In 100 per cent. there was increased or stationary systolic pressure; in 85 per cent. there was increased pulse pressure. In 15 per cent. stationary pulse pressure. In none, decreased pulse pressure. Group "fair" 85 cases, in 65 per cent. increased or stationary systolic pressure, in 35 per cent. decreased systolic pressure; in 41 per cent. increased pulse pressure, in 28 per cent. stationary pulse pressure, in 31 per cent. decreased pulse pressure.

Group "poor," 29 cases. In 41 per cent. there was increased or stationary systolic pressure; in 59 per cent. decreased systolic pressure; in 21 per cent. there was increased pulse pressure, in 21 per cent. stationary pulse pressure, in 58 per cent. decreased pulse pressure.

In the subdivision, for the purpose of emphasizing the main point, I have noted in terms of percentage only, cases in "fair plus" (+) and "fair minus" (−). It is to be remembered that "fair plus" signifies bordering on good, and "fair minus" signifies bordering on poor.

In the 17 cases recorded as "fair plus," there was increased or stationary systolic pressure in 77 per cent., decreased in 23 per cent., increased pulse pressure in 53 per cent., stationary pulse pressure in 29 per cent., decreased pulse pressure in 18 per cent. In the 11 cases recorded as "fair minus" there was increased or stationary systolic pressure in 9 per cent., decreased in 91 per cent., increased pulse pressure in 18 per cent., stationary pulse pressure in 36 per cent., decreased pulse pressure in 45 per cent.

Conclusions. In the estimation of myocardial efficiency, systolic blood-pressure and pulse-pressure variations together with changes in pulse rate in relation to postures and light exercise have positive value.

Under the test described an increase in systolic pressure together with a stationary or increased pulse pressure is suggestive of fairly good myocardial efficiency.

A decrease in systolic pressure together with a decrease in pulse pressure is suggestive of poor to bad myocardial efficiency.

While the cases reported do not furnish data for comparative study in the individual case, it is obvious that repeated applications of the test, under uniform conditions, should furnish in the individual case, evidence in relation to progress.

REVIEWS

Collected Papers of the Mayo Clinic, Rochester, Minnesota. Edited by Mrs. M. H. Mellish. Vol. VI, 1914. Pp. 814; 347 illustrations. Philadelphia and London; W. B. Saunders Company, 1915.

This the sixth volume of these collected papers is the first of the series to be numbered, and appears with a slightly changed title, no reference now being made to St. Mary's Hospital. This no doubt is to be explained by a wish to give public recognition to the fact that a fair proportion of the work here represented is done outside of St. Mary's Hospital, and by some who have no direct affiliation with it. Though this hospital is still the centre of the clinical work of the Mayo Clinic, there are several other hospitals or *sanatoria* in Rochester, in addition to the large clinic building—all of them quite distinct from St. Mary's Hospital, yet a part of the "Mayo Clinic."

A thought that has impressed itself in reviewing this volume, as it has in reviewing its predecessors, is this: Why is not the official status of each of the contributors to the volumes defined somewhere? It is undeniable that a comparatively unknown name carries more weight if there is some indication of the amount of personal experience which the writer possesses. For example: in the present volume there is a paper on the use of the Roentgen rays in the diagnosis of pulmonary tuberculosis; it is stated that it is based on the combined radiographic and clinical findings in a series of 1000 cases of pulmonary tuberculosis, but the writer's status in the Mayo Clinic is not indicated, and from the context cannot be inferred. Some of the other contributors refer glibly to the three, four, or ten or more thousand cases of a certain affection observed in "our clinic," when it is quite evident that they refer not to cases personally studied, but to the entire material of the Mayo Clinic since its origin. In the same sense just consider the hundreds of thousands of cases to which a newcomer could refer if writing as a representative of the Hôtel Dieu at Paris or the Allgemeine Krankenhaus at Vienna.

When one comes to look back over the work and progress of the Mayo Clinic, it seems that three more or less distinct periods can be recognized, which are an epitome of the development of the surgical mind. The earliest period may be considered one characterized by descriptions of technique. In few other clinics in the world have surgeons so thoroughly systematized the mechanical details of the operations in common use in abdominal surgery, particularly in the surgery of the stomach and duodenum. And no one who has given thought to the matter fails to recognize that the highest merit of any operation is that it shall be reduced to a type and become a mere mechanical procedure in which one step follows the other with clock-work regularity, without let or hindrance. When this has been accomplished and the mechanical details have become familiar to surgeon and onlookers alike, then the operation as an operation has lost its interest.

The second period of development, and that which naturally succeeds the merely technical period, is the period during which the immediate mortality and the end-results of operations are of paramount interest. This period lasted a long time in the Mayo Clinic; and though the questions arising from the immediate mortality have nearly all been answered, those relating to the ultimate results are not entirely settled.

The final stage of development is that during which interest centres in pathology—the causes and natural course of disease; and it is this period on which the Mayo Clinic is now entering. The present volume, for instance, contains a great deal of matter relating to the pathogenesis of gastric carcinoma, and though it is rumored that some pathologists in other parts of the country do not think the conclusions reached by those they consider the "amateur" pathologists of the Mayo Clinic are warranted by the facts presented, it is of value, nevertheless, to have aroused discussion, and to have made the professional pathologists see the necessity for giving reasons for the faith or lack of faith that is in them.

One word more may be permitted the reviewer in closing. He knows that comparisons are odious, yet a comparison between the two chief surgical clinics of the country in a measure imposes itself. There is another clinic in this country — that at the Lakeside Hospital, Cleveland, where the main interest in the clinic from the very beginning of its career has centred in questions of pathology and pathological physiology. The technique of operation has never been neglected, for nowhere else in the world, we firmly believe, are operative details so accurately and faultlessly accomplished; and the immediate and ultimate results of treatment are nowhere else so studiously observed nor so excellent; but both technique and mortality statistics have always been subordinated to the overwhelming interest in the pathology of disease as it presents itself to the surgeon. The Mayo Clinic has achieved Roman citizenship at the price of fifteen years of hard toil; but the Lakeside Clinic was free born. A. P. C. A.

Diseases of the Skin. By James H. Sequeira, M.D. (Lond.), F.R.C.P. (Lond.), F.R.C.S. (Eng.), Physician to the Skin Department and Lecturer at the London Hospital; in charge of Queen Alexandra's Department for Light Treatment; Consulting Dermatologist to the Radium Institute; Secretary of the British Section of the International Association of Dermatology and Syphilis, etc. Second edition; pp. 650; 48 plates in colors and 238 text figures. Philadelphia: P. Blakiston's Son & Co., 1915.

The author has made a careful revision of this attractive book and has added one hundred and eleven pages, four new plates in color, and sixty photographs in the text. The work has been made of greater value to the investigator by the addition of several photomicrographs. Ringworm has been brought scientifically forward by plates showing the characteristics of various cultures. The writer treats of his subject by chapter headings, insofar as it is possible, from the etiological point of view. Eczema and also syphilis are treated upon in separate chapters, rather than in the former edition, with other diseases. Urticaria pigmentosa has been removed from "tumors of the skin" and placed under "toxic eruptions." Piedra (trichosporosis) has been transferred from "diseases of the appendages" to "vegetable parasitic affections." A considerable number of conditions have been added, such as grain itch, leukemia cutis, larva migrans, eczematoid ringworm, tropical ringworm, recurrent erysipelatoid eruptions on the face, trichomycosis axillaris flava, and rubra et nigra.

There has been a considerable amplification of pellagra, sporotrichosis, carcinoma, and epithelioma. Syphilis has been brought up to date by the description of Noguchi's luetin reaction, the exact method of giving salvarsan, and its contra-indications.

Although the book is not as large as several other text-books on dermatology, the large number of photographs in colors, most of which are excellent, make the volume a valuable asset to those interested in cutaneous medicine. F. C. K.

Black's Medical Dictionary. By John D. Comrie, M.A., B.Sc., M.D., F.R.C.P. (Edin.). Fifth edition; pp. 858; 431 illustrations, 12 plates. New York: The Macmillan Company. London: Adam & Charles Black, 1914.

The appearance of a fifth edition speaks well for the popularity of this book, but it is important for the medical man especially to know just what its scope is. The "original intention," which "has been sedulously kept in view" in this edition, is the effort to "produce a work which would occupy a position somewhere between a technical dictionary of medicine and one intended merely for the domestic treatment of the commoner ailments." It is further "hoped that these articles will be found useful to district nurses, ship captains, dwellers in remote districts and others who may be called upon to treat the suffering in the absence of trained supervision."

When the book is judged in the light of what it purports to be, it is found to be an excellent compilation of well-known medical facts and descriptions of well-worn medical terms.

Judged in the abstract as a medical dictionary, it falls far short of perfection through its incompleteness.

By its purposeful omission of many of the less common medical words and many of those recently coined, it will as often disappoint as reward a medical man in its use.

In a general way the book seems to fall into that class of medical books whose chief attraction lies in short cuts to medical knowledge, of which the English seem so fond. A. A. H.

Medical Jurisprudence. A Statement of the Law of Forensic Medicine. By Elmer D. Brothers, B.S., LL.B., member of the Chicago Bar; Lecturer on Jurisprudence in the Medical and Dental Departments of the University of Illinois and in John Marshall Law School. Pp. 299. St. Louis: C. V. Mosby Co., 1914.

The contents of this book is the fruit of twenty years of study, practice, and teaching on matters of a medico-legal nature. Its writing was incited by the lack of a satisfactory book of reference for medical students in their study of the legal aspects of medical practice.

The author has devised a ready and interesting means for both the prospective and practising medical man's learning, just what his legal medical responsibilities are. To one who has not given the subject thought, it comes as a rather startling fact that as physicians we are unconsciously entering into numbers of definite contractural relations daily which, upon default on our part, have their legal redress. On the other hand it is comforting to be told just what comprises a complete fulfilment of these obligations and responsibilities. A knowledge of the patient's contractural status and his obligation is also valuable, and will give the physician assurance in standing on his rights.

In addition to this general information of every-day use to internist, surgeon, and specialist alike, medical matters with more special legal bearings are discussed. These include expert testimony, privileged communications, civil and criminal malpractice, insanity, wounds, blood stains, crimes, etc.

It may be that lessons learned from this book will forestall a future learning from the book of bitter experience. One sees, however, that the law has not been one-sided: it insists equally on the rights as on the responsibilities of the physician, and it behooves every medical man to know just what his rights are.

A. A. H.

Surgery of the Bloodvessels. By J. Shelton Horsley, M.D., F.A.C.S., Surgeon-in-Charge of St. Elizabeth's Hospital, Richmond, Va., etc. Pp. 304; 89 illustrations. St. Louis: C. V. Mosby Company, 1915.

The preface of this volume says: "It has been the aim of the author to present the scientific and the laboratory features of vascular surgery and particularly its practical aspects that may be of interest both to the surgeon and to the general practitioner. Therefore the treatment of hemorrhage, pathological and traumatic, and such subjects as aneurisms, thrombosis and embolism, congenital nevi, varicose veins, and hemorrhoids are described as well as the history and technique of suturing bloodvessels and transfusion of blood." An aim such as this requires the use of cannister or of shrapnel at close range to hit all the individuals for whom the discharge is intended. This is the weak point of the book. The only subjects which are described better than in other works relate to mere matters of technique, especially the suture and anastomosis of bloodvessels and the transfusion of blood. These chapters are excellent, the illustrations above the average, and the author speaks with authority born of ample experience, yet with pleasing modesty. It remains to be seen, whether the recent introduction of the method of transfusion by the aid of citrate solutions will entirely replace those here described. Most of the other subjects are treated quite superficially, both from the scientific and laboratory stand-point and from the purely technical side. The chapters on hemorrhage are particularly lacking in both respects. An example is found in the totally inadequate, indeed, we may say the dangerously inadequate, account given of Momburg's method of hemostasis. The best chapters, apart from those already mentioned, are those on thrombosis and embolism. Yet here again otherwise excellent work is marred by an attempt at all inclusiveness. Surely, it was not necessary in a work purporting to deal with the surgery of bloodvessels to include illustrations and elaborate descriptions of intestinal resection and anastomosis, although the ostensible excuse for such inclusion is found in the fact that these procedures may become requisite in cases of mesenteric thrombosis or embolism. Why not have described amputations which may be required in various lesions of the limbs which are included? A. P. C. A.

The Difficulties and Emergencies of Obstetric Practice. By Comyns Berkeley, M.A., M.D., M.C. (Cantab.), F.R.C.P. (Lond.), M.R.C.S. (Eng.), Obstetric and Gynecological Surgeon to the Middlesex Hospital; Surgeon, Chelsea Hospital for Women, Senior Obstetric Surgeon, City of London Lying-in Hospital, etc., and Victor Bonney, M.S., M.D., B.Sc. (Lond.), F.R.C.S. (Eng.), M.R.C.P. (Lond.), Assistant Obstetric and Gynecological Surgeon to the Middlesex Hospital, Surgeon, Chelsea Hospital for Women, etc. Second edition. Pp. 807; 302 illustrations. Philadelphia: P. Blakiston's Son & Co., 1915.

The authors have given in an almost encyclopedic form a description of and rules to govern the treatment of difficult and complicated cases in obstetrics. The affections of the various organs and body systems are taken up in order, and are followed by chapters on the diseases of the ovum, on hemorrhage, and on the various forms of dystocia and the abnormal puerperium. The well-written chapters on obstetric surgery embraces practically all operations performed during the process of reproduction. The diseases of the newborn child and the artificial feeding of infants are discussed in the concluding chapters.

That the scope of the book may be better recognized, it is noted that under diseases of the intestinal tract fourteen topics are discussed; under disorders of the nervous system there are grouped nineteen subheadings; the diseases and injuries of the newborn child include references to sixty-one conditions; we find a reference to ankylostomiasis, another to the marriage of first cousins. However, to those rare complications as hepatic abscess and rupture of splenic aneurysm during pregnancy but little space is given; we also find a full and reliable discussion of tuberculosis and syphilis. For obvious reasons no mention is made of the physiology and management of normal cases. Difficult labor is dealt with fully, all forms of fetal and maternal dystocia, and the methods for their relief being taken up at length. The authors mention six conditions where craniotomy in the living child is indicated. Probably only a few men possess fingers of the length of those on the hand illustrated in Fig. 156. The position of the hand illustrated in Fig. 169, portraying the operation of internal podalic version, is directly opposite that recommended in the text. The corkscrew position of a pregnant woman for routine examination, Fig. 1, must necessitate some considerable ability of orientation on the part of the examiner. Chloroform, favored by the authors in labor with cardiac disease, is not the anesthetic of unanimous choice among American obstetricians, who also do not wholly agree with the authors as to the value of routine vaginal douching after normal labors.

Apart from these criticisms the book will be found to be fairly descriptive, and certain to be a practical and valuable aid to every practitioner of obstetrics. P. F. W.

THE NEWER PHYSIOLOGY IN SURGICAL AND GENERAL PRACTICE. By A. RENDLE SHORT, M.D., B.S., B.Sc. (Lond.), F.R.C.S., Hunterian Professor, Royal College of Surgeons, etc. Third edition; pp. 256. New York: William Wood & Co., 1915.

THIS book is an interesting collection of the most recent work bearing upon problems in physiology of direct practical importance to the physician and surgeon. The light of modern research is utilized to explain many of the phenomena met with in common practice. Among the most important questions discussed are the relation of vitamines to the occurrence of nutritional disturbances, such as beri-beri, scurvy, and rickets; surgical shock; the growth of bone; ductless glands; clinical physiology of the alimentary canal; the hemorrhagic diathesis; acidosis and diabetes; nerve regeneration.

In many of the conditions discussed, fallacies are exposed by the ray of science and valuable suggestions for rational treatment given. Thus the book is not only of interest in the abstract, but should be a direct practical aid to the practitioner in his daily work. R. H. I.

PAINLESS CHILDBIRTH. By MARGUERITE TRACY and MARY BOYD. Pp. 316; 19 illustrations. New York: F. A. Stokes Company, 1915.

THE recent sensational exploitation of twilight sleep by means of department-store lectures and feature articles in the popular monthly magazines has been followed by its presentation in book form. The title suggests the Utopian dream of the gravid woman. In a more or less haphazard manner the authors have combined references to foreign and American medical literature, remarks and abstracts of discussions on the topic and narratives of personal experiences with the method by several women. Much space is given to a description of the maternity clinic at Freiburg, and one wanders through many pages in following the development of the Dammerschlaf. The last third of the book consists of translations of articles by Kroenig and Gauss on this method of analgesia-amnesia in parturition. The illustrations serve no purpose, portraying, for the most part, a healthy looking set of infants and children. The book can hardly be recommenced as a scientific, impartial, or convincing presentation of the subject. P. F. W.

Text-book of Local Anesthesia. By D. George Hirschel, Assistant in Heidelberg Clinic. Pp. 181; 103 illustrations. London: William Wood & Co.

The author has endeavored to write a comprehensive treatise on the subject of local anesthesia. He has, according to his own statement, attempted to sift out the chaff and retain the wheat. This he has accomplished, in the reviewer's opinion, too well. He treats fully and well the anatomical features, and the work is replete with many excellent anatomical and applied surgical cuts, with a special reference to the nervous anatomy and the regions supplied by each group.

The technique of administration, the actual area to be anesthetized, and the extent of the uses of the method are all fully laid down.

All of us know that novocain plus some adrenal extract is the best drug on the market for local anesthesia, but there are also other very useful drugs, which the author either mentions once or not at all, a mistake of his to term his work one on "local anesthesia" and not, "novocain" anesthesia. E. L. E.

Causes and Cures of Crime. By Thomas Speed Mosby, Member of the American Bar. Pp. 353; 26 illustrations. St. Louis: C. V. Mosby Co.

This is a very interesting book. The author attempts to treat in a popular style the causes and cures of crime. Naturally such a large subject can only be discussed in a sketchy manner in such a short book as this, yet it is so well done, that the reader gains an excellent idea of the subject.

The author throughout takes the point of view that the whole question is medical and not legal. In giving the various causes for crime, he first takes up the question of seasons and develops the interesting fact that hot weather seems to have an effect chiefly in increasing crimes of impulse, while in cooler climates crimes against property are most frequent. In discussing the social factors of crime he takes up the law's delay and the very important question of law-making, pointing out the fact that with each new law new crimes are created. City life is much more prone to lead to crime than country life. He then takes up the influence of newspaper publicity upon the causation of crime, citing the well-known Thaw case. It is an interesting fact that crime is less frequent in poverty stricken nations than in those that are prosperous. He takes issue with those who do not believe that religion has its influence on the cessation of crime and especially criticises the views of Lombroso. He points out that the "refinements of life corrupt while they polish the intercourse of the sexes. The gross appetite of love becomes more dangerous when it is elevated, or rather, indeed, disguised, by sentimental passion." A point of view which cannot altogether be agreed with. From this it can be readily seen that the book is interesting and well worth reading.

T. H. W.

RECREATIONS OF A PHYSICIAN. By A. STUART M. CHISHOLM, G.P. Pp. 328. New York: Putnam's Sons.

IN these days of bustle and hustle, recreation is imperative for the physician, though much be sacrificed in the obtaining thereof. The title of the book under review seemed to make a strong appeal, and it was immediately conjectured that here would be found practical suggestions for the busy doctor, suggestions as to play, and hence recreation, from one who had had not only the time to think and to write about the subject, but also to experience the recreations which he was to offer to us. One needs to read but a few pages to realize how far wrong this conjecture is, for the title, *Recreations of a Physician*, indicates a volume of collected essays, read and printed by Chisholm, presumably as a part of his recreation scheme. Therefore, far from receiving any helpful hints as to how to recreate, one is baffled by the thought that since these splendid essays are merely recreation pastimes, what must and should be the product of a mind at work?

The essays are ten in number, and are uniformly good, dealing generally with subjects of historical interest, as might be expected, when the author's name is recalled. The "Banquo" contains some delightful views on the various readings of Shakespeare's text, the explanation of corrupted passages by different commentators, and the emendations that have been proposed to clarify obscure portions of the text; but why it is called "Banquo" is incomprehensible, even after reading "The Symbolism of Names," the next essay. In this essay occurs a delightful tale by Quevedo of Pontius Pilate, which has the charm of being "new," not chronologically, but in the sense of narration.

To the reviewer's mind "The Inherent Spirit of Medicine" is the best essay. In it is a defence of the profession of medicine with an exposition of its ideals, which every practioner, but especially every medical student, should read. "The study of medicine is an entrancing subject; its practice requires an array of virtues whose mere contemplation staggers the mind. One must meet violence with gentleness, ingratitude with equanimity, insult with fortitude, slander with silence. The physician's life is a daily exemplification of the Goldern Rule. The very sensitiveness that inspires sympathy with pain and misery is a weapon in the hands of ignorance and malice wherewith they deal dreadful wounds which must be endured silently. Resentment can have no place in the physician's mind. Equanimity must be maintained in the face of misapprehension and abuse." The medical student needs no better vade mecum than this.

To those seeking recreation, to those desiring information, and to those eager for instruction, this volume of Chisholm is warmly recommended. E. H. G.

Hand-book of Pharmacology. By Charles Wilson Greene, A.B., A.M., Ph.D., Professor of Physiology and Pharmacology, University of Missouri; Member of American Association of Anatomists, American Physiological Society, etc. Pp. 396; 70 illustrations. New York: William Wood & Company, 1914.

This hand-book is a presentation of the subject of pharmacology in the restricted sense of that term. In it Greene does not discuss drugs in their relation to diseased conditions but only the reactions of the normal body to drugs and drug agents. In other words, he distinctly separates pharmacology from therapeutics just as physiology is separated from pathology. This, he claims, will enable the student, for whom the book is primarily written, to get the principles of the subject of pharmacology without being burdened and confused by a mass of matter on practical materia medica and therapeutics.

He classifies his presentation of the subject according to the physiological reactions of particular groups, devoting a single chapter to each group or series of drugs, and in each case detailing the action of only the characteristic one or ones. Except for a brief introductory paragraph on the history and chemistry of the drug in each case the entire chapter is devoted to the reactions of the normal body to the drug, these effects first being outlined in italics, then presented in detail, and finally concisely summarized. This arrangement has pedagogical advantages and makes the book convenient for ready reference. T. G. M.

Coxa Vara. By R. C. Emslie, M.S., F.R.C.S., Orthopedic Surgeon to St. Bartholomew's Hospital, London. Pp. 35; 34 illustrations. Oxford University Press.

This monograph of about ten thousand words is devoted to a scientific investigation of coxa vara. The facts here presented are based upon a clinical study of cases, anatomical specimens, and radiographic investigations. There is a brief discussion of the development of the neck of the femur and anatomical coxa vara. Adolescent coxa vara is clearly outlined, with a brief summary of the etiological factors, symptoms, and radiographic findings. Infantile coxa vara is briefly discussed and moderate emphasis placed upon the causative factors. The pathological findings, radiographic and histological, are the result of the author's personal work. The treatment of this condition as outlined by the author is comparatively brief, stress being laid chiefly upon correction by apparatus and operative procedures. Although this work is comparatively brief it has a decided scientific value. W. J. M.

Alveolodental Pyorrhea. By Charles C. Bass, M.D., Professor of Experimental Medicine at the Tulane Medical College, and Foster M. Johns, M.D., Instructor in the Laboratories of Chemical Medicine at the Tulane Medical College. Pp. 167; 41 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

The recent discovery of the cause of pyorrhea alveolaris and the intense interest that it has aroused makes particularly appropriate the appearance of a monograph upon the subject by the two authors who, independent of the investigations of Smith and Barrett, published, shortly after these authors, the result of their work upon the same line, showing that the Endameba bucallis is pathogenic. These two groups of investigators independently came to the conclusion that the organisms are pathogenic because of the favorable effects upon the lesions of the disease produced by the action of emetin. These results have subsequently been corroborated by numerous observers so that at the present time an annoying, disagreeable and sometimes serious disease has been deprived of much of its former power of harm.

The monograph is divided into nine chapters, of which those dealing with the etiology, morbid process, symptomatology, diagnosis, treatment, and prophylaxis are the most important. Probably the most interesting chapter is the one upon prophylaxis in which rather radical views are expressed as to the necessity of the tooth brush and of tooth powders.

The book can be recommended as an admirably complete and accurate summary of our knowledge of the subject. Its chief fault, perhaps, is the too obvious effort to spread out as much as possible the subject matter, to make the number of words as few to the page as possible, to make the print much larger than necessary and in fact to give the impression that a great deal more has been said upon the subject than is actually so. J. H. M., Jr.

Les Techniques Anatomo-pathologiques du Systeme Nerveux. Anatome Macroscopique et Histologique, par Gustave Roussy, Professor Agrege, Chef des travaux d'anatome pathologique a la Faculte de Paris, et Jean Lhermitte, Ancien Chef de laboratoire a la Faculte de Paris. Pp. 55; with illustrations. Paris: Masson et Cie., 1914.

This is a small volume devoted to the subject of neurological technique in the laboratory. The authors first treat of the method of hardening the brain, and describe Marie's method of cutting it. The methods of fixing, embedding, and staining the tissues are described in detail. Separate chapters are given to the subject of staining each element of the nervous system, the cell, axis-cylinder, neuroglia, etc. The authors are thoroughly conversant with the newest methods of staining. The arrangement of the book is excellent. A summary of the procedure is found at the end of each staining method. The book is a good practical manual to have at one's elbow in the laboratory. S. L.

Anatomy and Physiology for Nurses. By Amy E. Pope, Co-author of "Practical Nursing" etc. Pp. 554; 135 illustrations. New York: G. P. Putnams Sons.

At present, when the nurse plays so prominent a part in Social Service, it is important that she should understand the reasons for the orders that she gives and transmits to the patients in her care. For this purpose, the present volume, by reason of its completeness, is admirably adapted. It is attractively gotten up and would make an excellent text-book for any nurses' training school.

S. J. R.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Detoxication of Diphtheria and Tetanus Toxins.—J. Schumacher (*Deutsch. med. Wchnschr.*, 1915, xli, 310) reports the results of experiments he has performed to protect animals from fatal doses of diphtheria and tetanus toxins. Sieber has shown that abrin, diphtheria, and tetanus toxins can be rendered non-toxic by previous treatment with hydrogen peroxide. The latter substance is not suitable for intravenous use. Schumacher selected ammonium persulphate, which is also a strong oxidizer, for his experiments. It is relatively non-toxic. The experiments were performed upon guinea-pigs. The animals were given eight times the lethal dose. The controls all died within twenty-four hours after receiving the toxins. In a second series of animals, 2 c.c. of 5 per cent. ammonium persulphate was allowed to act upon the diphtheria toxin in the syringe for ten minutes before the injection was made. These animals showed no symptoms whatever. Intravenous administration of 2 c.c. of 5 per cent. ammonium persulphate solution ten minutes before giving the toxin delayed the death of the animal twelve hours. Similar results were obtained with tetanus toxin. A more detailed study of this question will appear in a later communication.

Leukopenia and Aneosinophilia following Typhoid Vaccination.—Frieda Schneider (*Deutsch. med. Wchnschr.*, 1915, xli, 393) confirms the findings of others to the effect that agglutinins for typhoid bacilli appear in the blood following antityphoid vaccination. She has found agglutination positive in dilutions of 1–160 to 1–320. This finding, of course, renders the Widal test of little value in suspected typhoid in those who have been vaccinated. The author investigated other blood changes found in typhoid fever, *i. e.*, leukopenia and aneosinophilia. Examination showed that both of these phenomena made their appearance within a few days after the third injection of typhoid vaccine and that they may persist for several months. This should be borne in mind in the investigation of vaccinated individuals.

Agglutination of the Spirocheta Pallida.—A. Kissmeyer (*Deutsch. med. Wchnschr.*, 1915, xli, 306) has investigated the possibility of an agglutinin formation in syphilitics, since the literature of the subject is rather contradictory. In studying human syphilitic sera, the author was able to demonstrate an agglutination in each stage of the disease, though the phenomenon was an inconstant one. He looks upon agglutination in dilution of 1 to 100 occurring after two to three hours in the incubator at 37° as positive. Occasionally, a non-syphilitic serum will cause agglutination in dilutions of 1 to 50. Most positive sera will also cause agglutination in dilutions of 1 to 100. In one patient in the primary stage of the disease, agglutinins appeared in the blood before the Wassermann reaction became positive. In congenital syphilis the agglutinin reaction was strongly positive in patients under twelve years of age. With increasing age there was a decrease in the intensity of the reaction. By injection of killed spirochetes into rabbits the author was able to produce sera having very strong agglutinating power. The effect of treatment on the presence or absence of agglutinins in the sera of syphilitics is under investigation.

The Bacterial Therapy of Typhoid Fever.—Encouraged by the reports of Ichikawa and of Kraus and Mazza, M. Rhein (*München. med. Wchnschr.*, 1915, lxii, 427) has tried the bacterial therapy on a series of thirty-three patients suffering with typhoid fever. He prepared his vaccine as follows: To 5 c.c. of Halle typhoid vaccine and 0.5 gm. pure phenol, physiological salt solution was added to a volume of 100 c.c. Of this preparation he employed 0.6 to 1.4 c.c. diluted with 8 c.c. physiological salt solution for intravenous injection. Within one to two and a half hours a rise in temperature and a chill of varying severity and duration (five to thirty minutes) occurred in 94 per cent. of the cases. Injections were made only in patients in whom the diagnosis was clear clinically or bacteriologically. Three of the patients treated showed paratyphoid bacilli A in the blood. Patients exhibiting the step-like curve of defervescence were excluded, as were also those suffering with complications such as pneumonia, pleurisy, nephritis, or myocarditis. Status typhosus, with delirium and bronchitis, but with good pulse, was not looked upon as contra-indication for injection of vaccine. Thirty-three patients received the injections and six of these had a second injection. In 9 cases there was a critical fall of temperature within one day after the first injection and in 1 case after the second. In 13 cases a favorable effect on the temperature curve was noted after the first injection and in 3 cases after the second injection. In 8 patients there was no effect whatever on the temperature curve, and in 2 of these a second injection was also without visible effect. On the other hand, 3 patients who were unaffected by the first injection reacted favorably after a second. In the 3 cases of paratyphoid fever a critical fall of temperature was not observed, but there was a gradual lowering in the fever. Of the patients injected, 3 died; in none could the death be attributed to the injection. Of all the patients treated, only 1 suffered from intestinal hemorrhage, which occurred six days after the injection. Other complications were not observed in the injected patients. No evidence of collapse even in patients with weak pulse was seen. The reaction of the patient to the injection was studied with relation to the following clinical signs or symptoms: Bronchitis, palpable spleen, roseola, Diazo reaction, leukocyte count, eosinophile count, and bacteriemia. A favorable response to the injection could not be correlated with any of these. However, after crisis, comparatively many eosinophiles (100 to 200 per c.mm.) appeared in the blood in twenty-four hours in spite of the leukopenia, and the Diazo test remained positive as long as three days after the temperature was normal. It was noticeable that with larger dosage (4 c.c.) the crisis was of shorter duration. Since no ill effects followed the injection, and, on the contrary, in 48 per cent. of the cases the fever was shortened and in 30 per cent. cure followed within two days, the author feels that in every case of uncomplicated typhoid fever, bacteriotherapy should be tried.

A Test for Antithrombin in the Blood.—There have been thus far but few estimations of the antithrombin content of the blood. Most of them have been made by Howell, who has used a method which he has devised, and though it is satisfactory, it is not simple and not suited to wide clinical use. The substances required in the test demand considerable experience in their preparation. Hess (*Jour. Exper. Med.*, 1915, xxi, 338), therefore, has devised a test, the chief advantage of which is its simplicity and the fact that it does not require a difficult preparation and maintenance in a pure state of fibrinogen and thrombin. The principle involved consists essentially in titrating the antithrombin against normal human plasma. The method briefly is as follows: 9 c.c. of blood are put into 1 c.c. of 1 per cent. sodium oxylate. The mixture is centrifuged and the plasma removed in the usual way. The plasma is then recalcified by adding 2, 3, 4, and 5 drops respectively to a 0.5 per cent. calcium chloride. By this method one ascertains the general coagulability of the plasma and the optimum amount of calcium for this particular plasma. It is well known that heating plasma to 60° C. destroys prothrombin and coagulates fibrinogen. If now this plasma is filtered the filtrate contains antithrombin, the strength of which can be ascertained as follows: some normal plasma is prepared in exactly the same way as is the oxylated plasma to be tested, 5 drops of which are put into five carefully cleaned vials. The first tube serves as a control. To the second and third tubes are added three and five drops respectively of normal antithrombin; to the fourth and fifth tubes equal amounts of antithrombin that is to be tested. The volume of all the tubes is made equal with normal salt solution. The tubes are allowed to stand fifteen minutes. The plasma is then recalcified by the addition of 0.5 per cent. calcium chloride. Antithrombin is judged to be in excess when a marked delay in coagulation is brought about in the tubes to which it has been added as compared to the coagulation in the control tube.

Report on the Allen Treatment of Diabetes.—Hill and Sherrick (*Boston Med. and Surg. Jour.*, 1915, clxxii, 696) report in the present article their results in a small series of cases of diabetes which have been treated according to the method recommended by Allen. In brief, their routine is to put the patient first on a house diet for two days, thus determining his tolerance for ordinary diet and the severity of his diabetes. On the third day the patient is put to bed and given nothing but black coffee with one ounce of whisky every two hours from 7 A.M. to 7 P.M. This diet represents an intake of about 800 calories. Provided there is much acidosis, as indicated by the amount of diacetic acid and acetone in the urine, sodium bicarbonate is given. Patients are kept on this regime until sugar-free. This usually requires from two to three days, during which time there is usually a slight loss of weight and relief from such symptoms as itching and excessive thirst. They have never observed any indication of acid poisoning in cases treated by this method. As soon as the patient is sugar-free he is given a single "vegetable day," after which the diet is slowly raised, increasing first the fat, then the protein, and lastly the carbohydrate. Fat is never raised above 200 grams and the caloric intake rarely above 2200. They emphasize three important things in the treatment: (1) not to worry if the patient loses weight; (2) not to raise the diet too quickly after starvation; (3) pay just as much attention to the protein intake as to the carbohydrate. Included with the article there is a series of diets which have been carefully figured out, particularly to meet the requirements of patients after they have left the hospital. These will no doubt prove valuable.

Uric Acid Excretion in a Case of Total Occlusion of the Pancreatic Duct.—When a patient in the medical service of the Johns Hopkins Hospital was found to have a complete absence of pancreatic secretion in the intestinal tract the idea was conceived by D. W. Atchley (*Arch. Int. Med.*, 1915, xv, 655) that by feeding thymus gland and estimating the increased output of uric acid in the urine the possible necessity of the pancreas to any stage of nuclear digestion could be conclusively demonstrated. The patient, therefore, was put on a purin-free diet, and for four days the uric acid was determined by means of the Folin-Schaeffer method. On the fifth and sixth days the patient was given in addition 150 grams of fresh calf's thymus with the noon meal. The results showed there was practically a quantitative recovery of exogenous uric acid, a finding which conclusively demonstrates that there may be digestion of the thymus nuclei, with the production of uric acid in the urine, in the absence of both bile and pancreatic juice. This finding as well as similar ones in other cases, definitely points out the worthlessness of the Schmidt-nuclear test for pancreatic function.

Renal Irritation in Relapsing Fever.—L. Jarno (*Wien. klin. Wchnschr.*, 1915, xxvii, 416) has studied the urine in a series of 170 uncomplicated cases of relapsing fever. Daily examinations were made and strikingly constant changes were found. The first day of the disease only a trace of albumin may be found in the urine. On the second day of the attack there is 0.5 to 1.5 gms. of albumin per liter, and at the same time numerous granular casts appear. During the first attack of fever these changes remain quite constant. On the third afebrile day, more rarely on the second, there is a gradual decrease in the number of granular casts and in the amount of albumin. By the fourth day the urine is again normal. The urinary findings in the second febrile attack are in every way similar to those in the first, and the urine also clears up in the afebrile period in the same way. If a third and fourth attack occur the albuminuria usually returns, but the granular casts are generally much less abundant than in the first two attacks. The albuminuria, however, disappears early. It seems evident that there is a severe renal injury at the beginning of the disease, but as the infection continues, the kidneys seem to become more resistant to the harmful agent. Exceptional cases were noted where the urinary changes were in some instances less pronounced, in others more severe. In one instance, chronic nephritis remained.

Vaccine Therapy in Typhoid Fever.—In answer to inquiries from Prof. Paltauf, Biedl and H. Eggreth (*Wien. klin. Wchnschr.*, 1915, xxvii., 125) have given their experiences with the vaccine treatment of typhoid fever. Paltauf publishes their letters in full. Biedl has treated a series of 22 cases of severe typhoid fever in the beginning of the second week; the blood culture was positive in all of these. Of this number 2 are excluded. Both were men with high fever, status typhosus, and recurring epistaxis, the last nose-bleed occurring one day before injection in each case. Two hours after injection of the vaccine there occurred in each patient an uncontrollable hemorrhage from the nose which led to death. Of the remaining 20 cases, 11 received Vincent's vaccine (typhoid bacilli killed with ether), first 100,000,000, later 250,000,000 to 300,000,000 in 2 c.c. of salt solution, and 9 were treated with Besredka's vaccine intravenously (sensitized living typhoid bacilli) in doses of 250,000,000 to 300,000,000 in 2 c.c. of salt solution. The end result was as follows: Of the cases treated with Vincent's vaccine there were 3 who died; 2 received subcutaneous injection and died fourteen and eighteen days respectively after the injection; 1 treated intravenously, after an initial favorable response died in the third week from severe bronchopneumonia and heart weakness. Evidently none of these deaths were due to the vaccine. The remaining 8 patients recovered. All of the patients treated with Besredka's vaccine recovered. Biedl's impressions were decidedly favorable. Following the intravenous injection there was a rise in temperature in one to two or three hours from 39° C. to 40° or 41° C., in one case even to 42° C., followed in twelve to eighteen hours by a critical fall of temperature to normal. No signs of collapse were observed; indeed, in two cases the injection was made when the patients were in a state of collapse with a pulse which could not be counted. Within three hours the temperature rose, the pulse became much fuller and 100 per minute. Following crisis the patients felt much better. The patients treated with Besredka's vaccine remained afebrile. Some of the other patients had slight evening elevations of temperature; in none above 38° C. Eggreth treated a series of 43 cases of typhoid fever with a single intravenous injection of 0.5 to 1.0 c.c. of Besredka's vaccine. Subcutaneous injections had produced no result. In 34 cases of Eggreth's series a critical fall of temperature followed within three to twelve hours after the injection, frequently with profuse sweating and marked relief of headache and delirium. Of these patients 31 remained afebrile; the remaining 3 developed fever after twelve, fourteen, and fifteen days, due respectively to endocarditis, to bilateral purulent parotitis, and to suppurative osteoperiostitis. The majority of the patients received the injection between the seventh and sixteenth day of the disease. In a group of 8 cases in the fourth and fifth week of the disease, suffering with broncho- or pleuro-pneumonia, the injection was ineffective. The forty-third case died three hours after the injection. An autopsy was performed which revealed typical typhoid lesions in the small intestine, pneumonia, and myocarditis. The patient had been brought to the hospital unconscious and desperately ill, and a poor risk. Paltauf utters a word of warning, as he has heard of a few instances of collapse following the intravenous use of Besredka's vaccine.

The Bacteriology of Appendicitis.—Rosenow (*Jour. Infect. Dis.*, 1915, xvi, 240) reports the results of his observations and experiments, which seem to indicate that appendicitis, in the absence of foreign bodies, is very frequently of a hemtogenous origin and secondary to some distant focus of infection. The organisms most commonly found in the distant foci are streptococci, and the disease develops when, for some reason or other, the organisms have acquired an affinity for the appendix and at the same time gain entrance into the circulation. These findings further bear out the author's theory that a focus of infection is to be regarded not merely as the place of entrance of bacteria, but also as the place where they may acquire the power necessary to infect distant organs and tissues. The importance is emphasized, therefore, of a thorough search for and removal of possible foci of infection, from which appendicitis may originate, and that this may occur in clinical experience is indicated by the not infrequent occurrence of the disease, at times almost in an epidemic form, when throat infections are particularly prevalent.

The Factors of Coagulation in Pernicious Anemia.—Drinker and Hurwitz (*Arch. Int. Med.*, 1915, xv, 733) have studied the various factors in a series of cases, including seven of pernicious anemia. They emphasize again the essential characteristics of this disease and especially those cases which are distinguished chiefly by failure to regenerate blood cells and by a tendency to bleed. In a typical case reported in full, they were able to note that the coagulation time was distinctly prolonged once only; that the bleeding time was always long, and that the platelets were always far below normal, nor were they consistently increased by transfusion. Antithrombin was consistently normal, as was fibrinogen, and neither was affected by transfusion, though this procedure tended to cause a slight transient rise in pro-thrombin, which was otherwise constantly decreased. This diminution in prothrombin is not great and is probably unimportant, provided active regeneration is in progress. The other normal findings occurred even in the presence of extremely low cell counts.

Nitrogen Metabolism in Dermatoses.—Tidy (*Quart. Jour. Med.*, 1915, viii, 129) gives a general review of the earlier studies and opinions upon this subject, as well as the results of more recent researches, which have been carried out particularly in cases of erythema, urticaria, and cases showing scaling or bullous eruptions. As a result of the investigations, it seems apparent that the changes in the nitrogenous excretion in various skin diseases are the result of the condition of the skin and are not connected with the cause of the disease. The retention of nitrogen is due to an abnormal nitrogen excretion by the skin, and changes in nitrogen excretion may precede the eruption as well as survive it. In view of these findings it is distinctly reasonable and advisable that a low protein diet be tried in these forms of dermatitis which are known to be associated with disturbances of the nitrogen excretion.

SURGERY

UNDER THE CHARGE OF

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The Treatment of Gun-Shot Aneurysms in Special Sites by Artificial Strengthening of its Walls.—Haberland (*Zentralbl. f. Chir*, 1915, xli, 281) reports a case of traumatic aneurysm due to a gun-shot wound at the junction of the external iliac and femoral artery, which increased in size slowly and was operated on ten weeks after the injury. The method employed applies only to peripheral aneurysms of moderate size. There must be many cases in which such an operation will preserve the continuity of the lumen of the injured artery, and prevent further growth and rupture of the aneurysm, as well as relieve the pain. In this case the aneurysm was 8.5 by 5 cm. in size, pulsated strongly and its upper border could not be clearly outlined by palpation over Poupart's ligament. A large skin flap was made with its base above Poupart's ligament and the aneurysm about in the middle of the exposed area. Care was necessary in the separation of the flap, as only thin scar tissue separated the wall of the aneurysm from the skin in the region of the gun-shot wound. A flap was made from the fascia external to the aneurysm with its base along the border of the aneurysm, large enough to permit it to be turned inward and easily cover the aneurysm. It was then fixed in position by close silk sutures and the skin flap sutured in position over it. Healing was good. Three months later no further growth of the aneurysm could be detected.

Disinfection of the Hands and Abdominal Skin Before Operation.—McDonald (*Surg., Gynec., and Obst.*, 1915, xxi, 82) says that his experiments show the germicidal strength of alcohol to be of no great value. Its virtue in cleansing the hands is exerted more as a chemical solvent than as a germicide. Though a solvent of free fatty acid, it will not dissolve the fat as found in the skin, *i. e.*, the glyceride. The ideal skin disinfectant should be a fat solvent. Alcoholic solutions of iodine give only superficial disinfection, while with solutions of iodine in fat solvents such as tetrachloride or chloretone, there is complete penetration, as has been shown by McDonald's carbon tetrachloride 2 per cent. iodine solution. During a period of ten years, McDonald has tried many hundreds of solutions and germicides and has compared one with another as to results. His final solution has the following parts: Acetone (commercial), 40 parts; denatured alcohol, 60 parts; and pyxol, 2 parts, the latter being the germicide. The method of disinfection advised is simply to treat the hand in this solution in a vessel sufficiently large to admit the hands and rub, with a nail brush for the nails and a gauze cloth for the arms, to aid the solution in permeating every crevice. The immersion should last one minute. This solution has the following advantages: It is reasonably cheap; does not irritate the skin; contains a fat solvent, acetone, causing the solution to penetrate; the alcohol is a good vehicle; the solution contains a strong germicide which is twenty times as germicidal as carbolic acid in equal strengths and this germicidal value is not impaired by the alcohol or acetone. It has the germicidal value of phenol in 40 per cent. solution (if such a solution could be made), plus the germicidal action of the solvent. McDonald has used it for more than a year with uniformly satisfactory results. In the sterilization of the skin of the abdomen, it is rubbed on for two minutes before operation after the patient is under ether without any preliminary washing. Since it is possible to sterilize the hands so thoroughly and in such a quick and easy fashion, there does not seem to be any further advantage in using rubber gloves, for the hands can be sterilized after contamination in less time than it takes to remove the contaminating gloves and put on a clean pair. Since he has not used gloves, McDonald has, however, fortified his skin by means of a hand varnish which he has described in another journal.

Report on Skin Disinfection by McDonald's Solution.—McMullin (*Surg., Gynec., and Obst.*, 1915, xxi, 87) had the field of operation prepared, if possible, on the evening before the operation, by shaving and washing with green soap, water and alcohol. It was covered with a dry sterile towel and left until the next day. At operation the site was treated by rubbing with McDonald's solution for about two minutes. The hands of the assistants and operator were prepared by scrubbing with soap water and alcohol, followed by two minutes' treatment with McDonald's solution. He has operated, with this preparation, on over 276 major cases, practically all laparotomies and hernias. In emergency cases the soap and water scrubbing of the operative field was dispensed with and only McDonald's solution used. In these cases there were 7 skin infections. Excluding those cases in which infection was obviously due to some extraneous causes, there remained but 3 cases in which there was any skin infection, which might be attributed to improper disinfection of the skin. From this analysis of his experience, McMullin believes this solution to be the most efficient for skin disinfection at our disposal at the present time. Healing under its use seems to take place more readily than under the iodine skin disinfection. McMullin believes that wound repair is accelerated by at least three days, when compared to that following the iodine skin disinfection. Applied to the skin of the hand, the solution is unirritating and is almost ideal as a skin disinfectant.

Sterilization of the Skin by McDonald's Solution.—Stanton (*Surg., Gynec., and Obst.*, 1915, xxi, 89) says that water, up to 10 per cent. or more, does not interfere with the action of the solution. Hence it is possible to use it on wet skin surfaces, such as those recently lathered for shaving, or the operator's hands after he has scrubbed them with soap and water. The solution is itself an excellent cleansing medium and so harmless that it can be used actually to scrub the patient, whereas tincture of iodine should not be rubbed in. It can be used before the patient is anesthetized without danger of complaint, as it is not irritating. It does not stain skin surfaces and dries very quickly, so that it is not necessary to protect peritoneal surfaces from contact with the skin, as in the case of iodine skin treatment. Stanton had only 2 infections in 240 otherwise clean cases, a record never before equalled in his work. During the year 1914 there was not one drop of pus collected in a clean case operated upon by him. Such results are significant and at least show that the method of skin preparation was efficient. Even more important was the fact that the wound healing was without evidence of chemical irritation, without peeling or blistering of the skin, and quite as rapid as that previously observed in simple alcohol-prepared incisions.

Pylephlebitis Complicating Appendicitis.—Babler (*Ann. Surg.*, 1915, lxi, 589) says that formerly it was customary to regard perforative peritonitis as the most frequent and grave complication of appendicitis, but with the almost practical elimination of perforative peritonitis, he believes that the most grave complication is pylephlebitis with multiple abscesses of the lung or of the liver. In any given case the diagnosis must rest on (1) the history showing that the appendix was the primary seat of trouble, (2) the shifting of the symptoms from the appendix to the hepatic region, (3) the progressive increase in the severity and character of the symptoms, (4) the repeated chills followed by high pulse rate and marked elevation of body temperature, (5) the jaundice, (6) the persistent pain in the hepatic region, (7) the urinary and blood findings, (8) the change of liver dulness, (9) the picture of marked toxemia, and (10) the absence of the signs and manifestations of extensive peritonitis. The prognosis is necessarily grave. Prior to the work of Körte and Franke the complication was regarded as practically always fatal. The prognosis depends on (1) the size, multiplicity, and location of the abscesses, as well as their accessibility from a surgical stand-point, (2) the time of their discovery and (3) the general condition of the patient together with the character and time of the treatment. The treatment is outlined as follows: The appendix should be removed, the infected lymphatics leading from the appendix to the liver should be incised and drained, and the liver should be exposed and the abscesses located and drained. The abscess or abscesses in the lung must be located and drained. The intense pain will frequently guide the surgeon to the site of the abscesses. Babler does not feel that it is advisable to aspirate the liver until the latter has been duly exposed, unless preparations for immediate intervention have been completed. He strongly supports the lumbar drain in these cases.

The "Tongue-Depressor" Gastro-enterostomy Clamp.—Gibson (*Ann. Surg.*, 1915, lxi, 604) illustrates a very simple clamp for gastric and intestinal anastomoses, consisting of three small pieces of wood, the ordinary wooden tongue-depressors, which are bound together by any suitable method, such as strong artery clamp, or, if more convenient, a sterile rubber band. These might be replaced by strips of cigar boxes. In his hands, both in experimental and clinical work, it has proven much more satisfactory than the Roosevelt, Bartlett, and other clamps used for this purpose. He has found it particularly satisfactory in doing a gastro-enterostomy, when it is desired to release the clamp in putting in the last mucous suture and the final peritoneal suture. Removing the rubber band allowed the tongue depressors to fall apart without further manipulation. By this method injury to the viscera is less likely to be produced. Two gastro-enterostomies and one entero-anastomosis have been successfully done with the aid of these clamps.

The Bone Graft Peg in the Treatment of Fractures of the Neck of the Femur.—Albee (*Ann. Surg.*, 1915, lxii, 85) says a large number of these fractures occur in individuals below the age of forty-five and fifty. The terms intracapsular and extracapsular are inaccurate and misleading and there is no object in classifying these fractures further than by the single term, "fractures of the neck." If any classification is used that of Stimson is by all means the best, *i. e.*, subcapital, or fracture through the neck, and fracture at the base of the neck. A strong autogenous bone peg, accurately fitted into a hole drilled longitudinally through the neck of the femur, with the fragments in good position, offers unquestionably the most ideal condition for the rapid and satisfactory union, in good position, of this fracture. The technic of the operation is as follows: The patient should be placed upon some traction table (Hawley) which will allow, simultaneously, abduction and traction. The point of the fracture is reached by an incision starting from a finger's breadth inside of the anterior superior spine and curved downward three to five inches along the inner border of the sartorius, which is retracted outward. The rectus femoris is retracted outward and the iliopsoas inward. All soft tissue is then cleared from between the fractured ends, which are curetted and freshened. The limb is now abducted and sufficient traction applied to bring the fragments into good apposition as determined by both sight and touch through the anterior wound. An incision two to three inches long is then made over and just beyond the great trochanter which is exposed. With a small hand drill the proper direction for the motor drill is determined by trial, as shown by observation through both wounds, the hole passing parallel to and through the centre of both fragments. The motor drill should be held ready for insertion into the tract of the hand drill as it is withdrawn by the assistant. The motor drill, which forms a hole three-eighths of an inch in diameter, is pushed through the distal fragment until the burr end of the drill appears between the fragments, as seen through the anterior wound. Just as the end of the drill is engaging the broken end of the proximal surface, a reading on the graduated drill shaft is taken at its entrance aperture in the trochanter, so that by making additional readings it can be determined how deep the capital fragment is being penetrated. By studying the roentgenogram, the length of this fragment can be very accurately determined, and hence the desired depth of the drill-hole obtained. When the fracture has occurred near the head and the proxinal fragment is consequently short, the drill-hole should extend close to the articular cartilage of the head. The drill is disengaged from the motor and left in place, to avoid any possible displacement of the fragments while the tibial graft is being procured. The crest of the lower portion of the tibia is laid bare, and an area of the desired shape and size is mapped out in the periosteum with a scalpel. The desired length of graft can be determined by the graduated scale on the motor drill. The cross section of the graft should be just large enough to be shaped into the peg when the dowel shaper is used. When the graft peg is ready, the drill is withdrawn from the femur and the peg inserted. The fit must be accurate because the dowel cutter is the counterpart of the drill used. The accuracy of fit is very important. Too tight a fit causes a pressure anemia of the surrounding cancellous bone. Too loose a fit, or an irregular, inaccurate fit, would not produce good fixation or favor an immediate bony union of graft to the host fragments. The deep fasciæ are approximated with interrupted sutures of No. 2 chromic catgut. The skin wound is closed with continuous suture of No. 1 chromic catgut. The limb is placed in abduction (Whitman) in a plaster-of-Paris spica extending from the toes to the axilla. Three weeks after the operation, windows are cut in the plaster, and the wounds dressed. The dressing should be replaced with cotton for the purpose of restoring the tension of the cast and retaining the fixation. The long spica should be continued for six weeks and followed by a short one for six weeks longer.

Cryptogenetic Peritonitis with Special Reference to the Mode of Infection of the Peritoneum.—Brunzel (*Deutsch. Ztschr. f. Chir.*, 1915, cxxiii, 233) says that an advance was made with the discovery of the Fränkel-Weichselbaum pneumococcus and the designation of these so-called spontaneous or idiopathic cases of peritonitis according to this, apparently, most common cause. But the new name, "pneumococcus-peritonitis," did not throw light on the mode of infection of the peritoneum. Other bacteria may be at fault as the streptococci and staphylococci. The term, cryptogenetic, is used here to designate those cases of peritonitis in which the cause is unknown or not definitely established. The most frequent cause found in the cases studied by Brunzel was the pneumococcus. He advises early operation, since the diagnosis cannot be made beforehand with certainty, although the prognosis is not good even with operation. The infection of the peritoneum occurs exclusively by the blood, in all probability. Therefore, the so-called idiopathic or cryptogenetic cases of peritonitis are more properly cases of metastatic peritonitis and the metastases should be regarded as suppurative from a general septic blood infection. The abdominal symptoms occurring in the beginning or during the course of a pneumonia may be regarded as the result of a peritoneal reaction to the flooding of the peritoneum with pneumococci. When the infection gains the upper hand of the peritoneal resistance, the peritonismus becomes a peritonitis. The cases reported as localized pneumococcus peritonitis are to be strictly differentiated from those of general peritonitis. The prognosis is more favorable and for the greatest part, at least, these cases are confused with abscesses of the space of Retzius, which may be metastatic by the blood path or the result of the breaking down and extension of the suppuration from an infected lymph node.

Neurolysis of the Brachial Plexus.—Mehler (*Deutsch. Ztschr. f. Chir.*, 1915, cxxxiii, 299) reports from his experience in the present European war, the following case in which a gun-shot wound is supposed to have passed through Erb's point in the brachial plexus (junction of fifth and sixth roots of the plexus), and was followed by a complete flaccid paralysis of the arm which is supposed to have been due to the rupture of the plexus at Erb's point. The soldier was wounded October 2, 1914, and admitted to the hospital October 9, 1914. The wound of entrance was at the upper inner angle of the right scapula, the wound of exit just above the clavicle at Erb's point. The right arm was completely motionless (flaccid paralysis). Sensation was preserved. On examination the right arm hung flaccid, active movements were impossible, slight finger movements were present and all reflexes were lost. There was no response to the galvanic or faradic current, from the brachial plexus or the individual nerves and muscles. The condition remained unchanged to the end of December. The region of the brachial plexus was exposed by operation, January 5, 1915. Above and below the clavicle, the plexus was widely and firmly adherent to the surrounding tissues and extended as a broad plate, indistinguishable from the surrounding tissue, and showed tense cords especially posteriorly and lateralward. The plexus was separated, in part bluntly, in part by dissection, and the wound closed. Primary healing followed. Examination on January 22, 1915, showed a weak response of the plexus to the faradic and galvanic currents. There was slight movement of the arm, beginning supination and improved finger movements. On February 13, 1915, the hand and finger movements were almost normal and in the elbow-joint there were slight flexion and extension. The deltoid showed mild contraction. Still further improvement was noted on March 24, 1915.

THERAPEUTICS

UNDER THE CHARGE OF

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The Medical Treatment of Peptic Ulcer with Especial Reference to the Lenhartz Treatment.—Blumer (*Johns Hopkins Hosp. Bull.*, 1915, xxvi, 127) discusses the subject of the medical treatment of gastric ulcer, referring especially to the various diets as advocated by Leube, Lenhartz, Strauss, Jarotsky, and others. He believes that most patients with acute peptic ulcers, those with hemorrhage of the fulminating type and those with uncomplicated chronic ulcers should have the benefit of a carefully regulated and supervised medical regimen before being submitted to the knife. Ulcer patients with acute perforation, those with pyloric obstruction even in the early stages, those suffering from the results of repeated small hemorrhages intractable to medical treatment, and those with subphrenic abscess, hourglass stomach, or serious perigastric adhesions are best treated surgically. Blumer says that the contrast between different methods of medical treatment lies essentially in differences in the diet. A strict classification upon dietetic grounds is not entirely possible but three fairly sharply defined groups of diets can, however, be recognized; one in which more or less complete abstention from mouth feeding is the predominant feature, typified by the Leube cure; one in which immediate feeding with albuminous food is the essential peculiarity, typified by the Lenhartz diet; and one in which fats constitute the important source of nourishment, typified by the diets of Strauss and Jarotsky. The essential features of the Leube treatment are: Rest in bed; the daily use of luke-warm Carlsbad water; the application of hot poultices and Preissnitz compresses to the epigastrium; and a diet mainly of milk in increasing quantities, fortified after ten days by the addition of cereals and finally by meat. In bleeding ulcers the diet is preceded by several days of starvation, with nutrient enemata, an ice-bag to the epigastrium, and adrenalin, bismuth, and morphin medication. The principle underlying this diet is that to encourage healing of the ulcer the stomach must be spared from work as much as possible, and that in bleeding ulcers the organ must be given complete rest for a time. Modifications of the Leube diet have taken two opposite directions. On the one hand, starvation as a means of resting the stomach is carried to extremes by Rolleston, Wynter, and others of the English school of clinicians. On the other hand, diets advocated by Einhorn, Albe, and Boas increase the caloric value of the Leube diet by the addition to it of easily digestible and non-irritating nutriments. The essential features of the Lenhartz regimen consists of absolute rest in bed for at least three weeks, an ice-bag to the epigastrium until no occult blood appears in the feces, the routine administration of bismuth in all patients and of soft Blaud pills in anemic patients, and a non-irritating and non-stimulating diet of concentrated albuminous food given by the mouth from the onset of treatment and gradually increased in caloric value. The principles underlying this diet are: First, the hyperacidity plays an important role in preventing healing and that free acid must be neutralized by acid-binding food; and second, that the general nutrition must be maintained and anemia must be combated to favor healing of the ulcer. This diet has been frequently modified but only in non-essential details. Two diets which have apparently not been widely used, and which are based on the high caloric value of fats and their power to inhibit gastric secretion, are those of Jarotsky and Strauss. Jarotsky's diet consists of white of egg and olive oil given separately, several hours apart, in increasing daily amounts. Strauss uses a mixture of cream and yolk of egg either beaten up with sugar or rubbed up with butter. Blumer notes various objections to these diets as raised by different observers. The one great objection to the fat cures (Strauss, Jarotsky) is the inability of most patients to tolerate the large quantities of fat which they contain. The objections to both the Leube and Lenhartz treatment have been numerous. The best answer to the objections to the Leube treatment lies in Leube's record of 627 patients with a total mortality of 0.3 per cent., and a mortality in bleeding cases of 2.5 per cent. Only 1 per cent. of his patients showed no improvement under treatment, and 90 per cent. showed complete relief of symptoms on discharge. Lenhartz's 295 patients were all subjects of bleeding ulcer, and both his subjective cures and his mortality (2.3 per cent.) are almost identical with the results of Leube. Fewer recurrences of the bleeding during treatment seem to occur with the Lenhartz method than with the Leube. Blumer notes his personal experience with the Lenhartz diet in 27 cases treated with unessential modifications of the diet. In general he found that the diet was, as a rule, eminently satisfactory from the patient's point of view. The pain usually disappears within a few days. The patients seldom complain of hunger, and although most patients lose weight during the first week or ten days, many more than regain this initial loss before the treatment is ended. Thirteen of the patients reported by Blumer were suffering from the symptoms of duodenal rather than gastric ulcer, and 10 of these were entirely free from symptoms or signs of the disease at the end of treatment. All were benefited, there being no absolute failures. Five of them have remained well for over a year and a half. Of 14 gastric cases, two were not benefited at all, and four relapsed after a comparatively short interval. Blumer believes that patients with gastric ulcer do less well on the Lenhartz diet than those with duodenal ulcers. He is of the opinion that ulcers near the pylorus tend to heal badly, while bleeding ulcers seem to heal unusually well. Many ulcers would doubtless heal on complete rest, plus any of the dietary regimens that have been discussed. The tendency to adhere too closely to a particular form of diet is to be condemned as there are good points in all of the diets. The different regimens should be modified or combined in such a way as to suit the needs of the individual patient. The author gives the details of the various methods of dietetic treatment in his article.

Artificial Pneumothorax.—Leut (*Jour. Amer. Med. Assn.*, 1915, lxiv, 1973) sums up the indications for and the contraindications against the induction of an artificial pneumothorax for the treatment of pulmonary tuberculosis. He says that the ideal case is one in which the disease is limited to the upper portion of one lung, an acute progressive condition, generally with signs of softening, but which has not responded to the usual therapeutic measures. The treatment is indicated in cases with marked involvement of one lung, with a moderate infiltration of the opposite lung, preferably the apex. Artificial pneumothorax has often given brilliant results in cases of severe and uncontrollable hemorrhage. Some cases of pulmonary tuberculosis complicated by pleurisy with effusion, offer an excellent opportunity for giving compression treatment. Lung abscesses and bronchiectasis are occasionally benefited. Complications, such as tuberculous laryngitis or enteritis, may improve if the patient is doing well otherwise. The chief contra-indications are as follows: An extensive or progressive lesion in the opposite lung, or a disseminated miliary tuberculosis would preclude the gas treatment. The treatment would not be justifiable in patients even though far advanced who are doing well under the usual therapeutic measures. Generally, basal lesions in the opposite lung are contra-indications and are less favorable in the collapsed lung. Endocarditis and nephritis would lessen the chances of recovery in proportion to their severity. While dense pleural adhesions could not, strictly speaking, be considered contra-indications, they are nevertheless the chief cause of a large percentage of failures. Lent notes some of the complications that may follow the induction of artificial pneumothorax. Pleurisy with diffusion may occur in as high as 50 per cent. of the cases. This complication, though rarely serious, is an annoying one. The fluid persists for a long time, but generally should not be removed unless causing serious symptoms. The fluid may then be withdrawn and nitrogen gas introduced in its place. Tuberculous pyopneumothorax occurs in a small percentage of these effusions, but does not necessarily give a bad prognosis under the expectant treatment. Some cases of secondary infections have been reported, in which cases the outlook must be regarded as very serious. Numerous cases of shock following the operation have been reported. This can probably be avoided by careful cocainization of the tissues and by a preliminary injection of morphin. The danger of gas embolism is remote with proper technique. Emphysema, superficial or deep, may be encountered, but rarely produces any serious symptoms. Puncture of the lung followed by slight bleeding, may occur, but generally does not give rise to any serious symptoms. Dilatation of the heart is a serious complication, and is usually due to too great intrathoracic pressure. Care in gradually inducing the pneumothorax to permit the heart to accommodate itself to the increased pleural pressure should obviate this possibility. More or less severe pain caused by breaking up of pleural adhesions may also be mentioned among the complications. In his conclusions, Leut states that it is most gratifying that at last we have a rational treatment that may be used in the far-advanced cases. A comparatively few years ago symptomatic treatment, with the hope of temporary relief, was the only one given. The present status of artificial pneumothorax is that in a fair percentage of these hopeless cases we can offer either an arrest of the disease, or a chance of returning to good health. The procedure is attended with slight dangers, but these are insignificant as contrasted with the fatal outcome if the disease is allowed to go on unchecked. The duration of treatment is a question offering the greatest problem. It is impossible to determine whether the tuberculous foci in the collapsed lung have become entirely cicatrized, even though the patient is clinically well. It is far better to continue the treatment for an indefinite period, extending over years, than to discontinue the compression and discover after a few months that the disease is becoming active again, and when an attempt is made to readminister gas, that the layers of the pleura are densely adherent.

The Treatment of Leukemia.—HAHN (*Therap. Monatsh.*, 1914, xxviii, 555) says that during the past few years there has been a greatly increased literature dealing with the treatment of leukemia and that considerable discrepancy of opinion exists among different observers. From a study of the literature and his own observations the author gives his views regarding the present status of the treatment of leukemia. He believes that leukemia should be vigorously treated only where there is a severe and progressing anemia, the presence of large leukemia tumors or a great increase of the white cells. It is now recognized that many cases of leukemia suddenly show a marked aggravation of the disease even when apparently doing very well under some form of treatment. The relapse in such a case may prove far worse than the disease originally was when treatment was begun. With regard to the different methods of treatment, the author states that the Roentgen-rays seem to check the activity of the tissues producing white blood cells, but overdosage may prove fatal, and too small doses may actually stimulate the production of white cells. The stimulating effects of Roentgen-rays on the production of white cells have been observed in professional roentgenologists; Kimecke has recently reported six cases of leukemia developing in Roentgen-ray workers as a result of long-continued exposure to the rays. Hahn advises systematic exposure of every accessible gland in lymphatic leukemia, but in myeloid leukemia exposure of the enlarged spleen alone is effectual. In cases resistant to the treatment, benefit may be obtained by exposing the long bones of the legs between series of other exposures. He notes a marked improvement in 75 per cent. of his cases, while the others were not influenced. Béclère has reported no failures in 12 lymphatic and 93 myeloid cases and still others report very favorable results. Lymphatic leukemia seems less influenced by roentgenotherapy than myeloid leukemia, and almost invariably relapses. The effect of radio-active substances seems to be very similar to that derived from the Roentgen-rays. Radio-active substances fail in about 20 per cent. of the cases, according to the cases reported in the literature. Hahn found a great difference of opinion regarding beneficial effects of benzol therapy. He says it should not be given with coexistent disease of the liver or kidneys or when catarrhal intestinal inflammation exists. The consensus of opinion is that its use should not be continued till the leukocytes fall to normal numbers but that it should be discontinued when the leukocytes have dropped to 20,000 or 25,000. Hahn says that combined treatment is often very effectual especially a combination of benzol and roentgenotherapy. When combined, both can be used with lesser dosage. His experience has been that better results are obtained when treatment is begun with the Roentgen-rays and continued with benzol, not giving more than one gram a day of the latter. If myeloblasts appear in large numbers under roentgen treatment he changes to thorium X and follows with vigorous treatment with arsenic. In case of flaring up of the leukemia while under roentgenotherapy arsenic should be given a trial. With acute leukemia all treatment seems to be hopeless, but as it is not always possible to differentiate the acute form Hahn advises the trial of thorium X combined with a vigorous course of arsenic.

Experiences of the New York Board of Health in Typhoid Immunization.—Harris and Ogan (*Jour. Amer. Med. Assn.*, 1915, lxiv, 3) say that accurate observations recorded in hundreds of thousands of cases leave no doubt as to the preventative powers of antityphoid vaccination in all but a relatively insignificant number. In those few cases subsequently affected, vaccination strikingly decreases the morbidity and the mortality. Severe reactions are rare, but in order to avoid such reactions it is necessary to carefully observe certain precautions. Antityphoid vaccine should never be administered to any but the healthy. In order to permit of slow absorption the puncture of a vein, or intramuscular injection must be avoided. Children especially should avoid exposure to the sun following the administration of the vaccine. Antityphoid vaccine should not be given during the menstrual period or during pregnancy. No hard work or indulgence in alcohol should be allowed after the injection. Care should be taken not to reinject the vaccine in indurated areas. The authors state that when the incubation period has begun, the time for antityphoid vaccination has passed. Long and continued exposure to overwhelming doses of typhoid bacilli (in those who are in close contact with cases and especially in epidemics) may nullify the immunizing process of antityphoid vaccine, and an attack may therefore follow one or more injections. In fact antityphoid inoculation seemed to hasten the onset in cases cited by the authors. Chronic illness such as tuberculosis as well as debility or fatigue from other causes predisposes to severe reactions. The disease may develop after a complete immunizing course of treatment, in exceptional instances in which debility and fatigue exhaust the defensive powers of the body, and when exposure to massive doses of typhoid bacilli exists.

The Treatment of Typhoid Bacilli Carriers.—Gerome and Lenz (*Berl. klin. Wchnschr.*, 1915, lii, 341) were able to render the stools free of typhoid bacilli in three men, who were apparently becoming chronic carriers by giving thymol in combination with animal charcoal. Thymol was selected as an efficient disinfectant and the charcoal was combined with it on the theory that the charcoal would absorb the thymol and thus inhibit its absorption by the tissues and permit it to act as an intestinal antiseptic for a longer period of time and over a greater portion of the intestinal tract. This theory seemed to be confirmed by the urinary examinations which denoted much slower absorption of the drug. The thymol and charcoal were given in doses of one gram each three times a day; the charcoal half an hour before meals and the thymol half an hour after meals. These doses were continued for from one to two weeks. The bacterial content of the stools of normal individuals was tested after charcoal alone and after thymol alone and showed a distinct reduction but the diminution in bacteria was far greater when they were given together. The authors are of the opinion that this method is an efficient way of inducing intestinal disinfection.

OBSTETRICS

UNDER THE CHARGE OF

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The Disinfection of the Skin Before Operation.—At a Meeting of the Obstetrical Society of Berlin, Franz (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) stated that the use of the sterile rubber glove had solved the problem of disinfecting the hands. The question still remains as to what should be done with the skin at the field of operation. We may recall the elaborate methods which have been tried, consuming from twenty minutes to a half hour. The use of iodine has made such disinfection much shorter and less complicated. Franz compares the results obtained by the use of iodine in disinfecting the skin at the field of operation during one year. There were 273 abdominal sections, and as some were Alexander operations with double incisions there were 334 incisions. The mortality was 5.4 per cent. Perfect healing without secretion occurred in 81.7 per cent. Wound abscess formed in 6.9 per cent., and there was secretion in the wound in 6.6 per cent.

He compares these results with the work of another year, in which the following method was used: On the day preceding operation, the patient had a very thorough general bath. In some cases the abdomen was cleansed with cotton dipped in alcohol. No other local disinfection was practised. In this series there were 324 abdominal sections, with 81 Alexander operations, the latter making 405 incisions. The mortality was 4.6 per cent., while 85.9 per cent. of the cases had perfect healing without complications. Abscess formed in the wound in 8.1 per cent., and there was secretion in the wound in 3.3 per cent. When the two series are compared the results are all in favor of the bath and occasional alcohol method only, except in the occurrence of abscess in the wound. By the iodine method there was a smaller percentage than by the other, but this is counterbalanced by the fact that in the simpler method secretion occurred much more rarely in the wound. In discussion, Fromme described experiments which he had made upon some of the pregnant smaller animals to obtain their young in absolutely sterile conditions. To do this the young were delivered by Cesarean section, in a carefully sterilized room, and were then fed upon sterile food to avoid any possible contamination with bacteria. The young so delivered were stronger and grew much faster than those born in the ordinary way. The room was so constructed that manipulation could be performed with the hands covered with rubber gloves, without admitting air which contained bacteria. The further experiment was tried of making abdominal incisions upon these sterile animals to determine the healing of the wound. When the stitches were removed the wounds were found perfectly clean, but the edges were not in immediate apposition. The result would indicate that some bacteria are a benefit to the healing of the wound. Jolly recalled Olshausen's habit in cases of recently-ruptured, ectopic pregnancy, to operate without preparing the abdominal wall at all, and simply pour alcohol over the instruments. The results were excellent. No patient died of septic infection, and the wounds healed without complications. Jolly believed that the skin at the umbilicus was most dangerous through retained secretions and bacteria. Hammerschlag had tried applying wet dressings of bichloride solution to the abdominal wall for twelve hours preceding operation. He had seen one fatal bichloride poisoning as a result. Bumm had noticed that with the same precautions a series of cases would proceed with excellent healing of abdominal wounds, and then would come a series where stitch abscess and other complications would arise. At times in a Clinic nurses and physicians show a tendency to suppurating eruptions of the skin. Bumm described this to be the gradual development of bacteria in the hospital itself, and especially where cases were brought in infected, or where malignant growths proceded to suppuration.

Abdominal Cesarean Section Under Local Anesthesia.—Webster (*Surg.*, *Gynec.*, *and Obst.*, May, 1915) adds three others to his list of cases of Cesarean section under local anesthesia. The first patient had been in labor twenty-four hours and was somewhat exhausted, the fetal head very hard, large and above the pelvic brim, the cervix dilated. The operation was successful, the child weighing nine pounds, ten ounces. The patient remained quiet throughout the operation. The second patient was a girl of thirteen years and some months at full term pregnancy, the head to large to pass the pelvis. The child weighed eight pounds, three ounces, and the mother remained quiet during the operation. The third patient had placenta previa and pulmonary tuberculosis. Novocain was used with her, and to prevent further impregnation, the Fallopian tubes were divided. The results were satisfactory. He also reports the case of a woman who had a hernia of the fundus uteri. The hernial sac which was composed of the fundus was about three inches wide, on the left of the middle line, rising about an inch and a half above the level of the uterine wall. When the uterus contracted the hernia was made more prominent by the amniotic liquid forced into it. On section the hernial portion was removed, as it was only one-eighth of an inch thick. He also performed section under local anesthesia upon a woman, who, in a previous pregnancy had fallen on a bread knife which had perforated the anterior abdominal wall and uterus, necessitating an abdominal Cesarean section. Within two months of this operation she again became pregnant. At the second operation, the uterine incision was made two inches from the old scar and parallel with it. The old incision was found very thin and the tissue was dissected out to secure good union. To prevent the pain of infiltration for local anesthesia caused by the introduction of the needle, Webster has given nitrous oxide gas. In this way infiltration can be performed without haste and large areas of the skin rendered without sensation.

Anesthesia in Labor by Nitrous Oxide Gas.—Webster (*Surg., Gynec., and Obst.*, May, 1915) describes the use of nitrous oxide gas alone, or mixed with oxygen, 3 per cent. With the use of a small inhaler that covers the nose alone during the pain of contraction, sufficient gas may be given to abolish consciousness without lessening the pains. This method is used during the second stage, the anesthetic is withdrawn between the pains. The expense need not exceed $15 for any case, and may be reduced to about $5, with care.

Nephrectomy During Pregnancy.—Harrigan (*Surg., Gynec., and Obst.*, June, 1915) describes the case of a patient, four months advanced in her first pregnancy, who had an alveolar abscess. This ruptured spontaneously, but the patient developed a chill with high fever. Examination of the blood revealed a very high leukocytosis and the symptoms pointed to unilateral hematogenous infection of the kidney. Accordingly the right kidney was removed and found to be the site of multiple suppurative infection. The patient went on in pregnancy until seven and one-half months, when an attack of toxemia developed, and labor was induced and a viable child was born, which survived. Two years after the patient was in excellent health and apparently suffered no inconvenience from the loss of the kidney. Harrigan has collected 36 cases from the literature, and among these the ultimate result is stated in 30, of whom 28 recovered. Of these 20 went to labor without accidents or complications. Two aborted, and in two abortion was induced. Should the indications be present the obstetrician need not hesitate to remove the kidney from a pregnant patient. The reviewer has seen several women having but one kidney pass through pregnancy and labor successfully. In one instance a woman whose kidney had been removed for tuberculous infection and was without adequate care during pregnancy, had eclampsia from which she recovered.

The Duration of Pregnancy.—Peters (*Zentralb. f. Gynäk.* No. 17, 1915) discussed this subject before the Obstetrical Society of Vienna. He calls attention to methods already in use for estimating the duration of pregnancy, which fix the average at 270 days. In comparative studies with cows, in over 3000 cattle, the average was 284 days, with a variation between the longest and shortest pregnancies of 72 days. He quotes observations in Winckel's Clinic, where in 16,000 labors pregnancy in 31 cases had lasted from 302 to 322 days; in 12 cases 291 days. In the general series, in 71 per cent. pregnancy had lasted more than 280 days after the termination of menstruation, and in 62 per cent. pregnancy lasted over 270 days after conception. In general from 2 to 3 per cent. of pregnancies were considerably prolonged. The weight of the child increased in proportion to the length of pregnancy. As an aid in estimating the duration of pregnancy it must be remembered that ovulation occurs from fifteen to nineteen days after the beginning of the last period and from thirteen to nine days before the beginning of the next period. The average period of pregnancy after conception must be taken as practically 270 days. If we calculate more closely upon these data the average duration of pregnancy is from 261 to 268 days. It must be remembered that variations in the nutrition of the fetus play an important part in the duration of pregnancy, also variations in the type of menstruation in the mother. The influence of season, climate, race, and many other incidental factors affect this problem. In discussion, Schauta believed that the best method of practical reckoning was to consider pregnancy as enduring 270 days after conception and 280 days from the last period. He draws attention to the many difficulties in exact computation. He would take the first day of the last period, record the day of labor, and from this sum total of days subtract 18 or 19. This would give the probable time of pregnancy.

The Effects Produced by Placental Extract.—Colle (*Ann. di Ostet.* No. 4, 1915) has experimented with placental extract by injection into animals. He finds that when placed directly in the circulation it causes toxic symptoms, that when introduced into other channels of the body, this toxic element is absent. When injected into the veins it causes increased coagulation. It produces a lessening of blood-pressure of variable duration without excitement of the vasomotor centre. It has a tendency to lessen the respiratory rate and has little influence upon the heat centre. In a normal pregnant patient it does not bring on premature labor, but may stimulate the occurrence of labor at term. The maternal portion of the placenta is less active in its results than the fetal portion. The blood obtained from the placenta has the same effect as placental extract. When placental extract is made before the placenta has been thoroughly washed of all soluble material the extract is more efficient than if the placenta had been cleansed of its products. The efficiency of placental extract is in inverse proportion to its concentration. Putrefactive changes in the placenta diminish the efficiency of its action. The nitrogenous contents of the placenta vary in different cases and with different species of animals. Experiments show that the effect produced by placental extract may vary greatly in different cases. The effect upon an animal varies considerably with the rapidity of injection, for the rapid introduction of a large quantity of placental extract may prove fatal. In these cases no evidence of thrombosis or embolism is found. When placental extract is subjected to the action of the centrifuge there seems to be no essential difference in the material obtained.

The Delivery of the Placenta.—Kirkpatrick (*Jour. Obst. and Gynec. Brit. Emp.*, January, 1915) writes concerning methods employed to secure the delivery of the placenta. He finds that in 1767 Harvie published a pamphlet in which he called attention to the danger of pulling upon the cord, and recommended pressing downward and toward the pubes upon the uterus to expel the placenta. This method was not the Credé method, in that it did not compress the uterus from before backward, but it was a great improvement upon the delivery of the placenta by pulling upon the cord, and foreshadowed the Credé method.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF
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The Schick Reaction.—SCHICK, of Vienna (*Münch. med. Wchnschr.*, November 25, 1913, 2608), and PARK, of New York (Park, Zingher, and Serota, *Arch. Pediat.*, 1915, xxxi, 481) find that the blood serum of about 80 per cent. of the newborn, from 50 to 60 per cent. of children, and 90 per cent. of adults contains sufficient diphtheria antitoxin to protect them against diphtheria. A positive Schick reaction is sufficiently delicate to indicate less than $\frac{1}{30}$ of a unit of antitoxin in 1 c.c. of blood serum. Such persons are susceptible to diphtheria. The Schick reaction consists in injecting $\frac{1}{50}$ of a minimum lethal dose of diphtheria toxin for a 250-gram guinea-pig into the skin. BUNDESEN (*Jour. Amer. Med. Assn.*, 1915, lxiv, 1203) concludes as follows: (1) By means of the Schick test we are in a position to tell definitely who is susceptible to diphtheria and when an epidemic breaks out can inject those and those only, paying no further attention to the one giving a negative reaction. (2) By it the danger of cross-infection is greatly decreased. Children with diphtheria that have had scarlet fever and are therefore immune from scarlet fever can be placed in scarlet fever wards when the inmates yield negative Schicks, etc. (3) It permits a great reduction in antitoxin bills. Much needless pain and annoyance of patients is avoided and the possibility of anaphylactic shock is greatly minimized. GRAEF and GINSBERG (*Jour. Amer. Med. Assn.*, 1915, lxiv, 1205) conclude as follows: (1) The most susceptible age is between one and five years. (2) Immunity obtained by having the disease or by the use of immunizing doses of antitoxin lasts from a month to several years, varying greatly in different individuals and being very brief in children. (3) The Schick test is a helpful agent in testing the efficiency of immunization by antitoxin as well as the natural immunity existing in many persons. (4) It has helped to place on more certain grounds the assurance that bad cases of diphtheria should receive early and large doses of antitoxin by intravenous injections. Antitoxin is ten times as effective when so used, as compared with the ordinary methods of administration. (5) Park has obtained results in families showing a striking similarity in reactions to the test. If the youngest child of a family has a negative reaction, all the older children are likely to be negative, and if the older children are positive, the young ones are also. When variations are found, the younger children show the positive reaction. MOODY (*Jour. Amer. Med.*

Assn., 1915, lxiv, 1206) concludes as follows: (1) The test is of definite clinical value in differentiating between persons who are susceptible to diphtheria and those who are not susceptible, and is therefore useful in determining which cases, of those to be placed in an environment where the liability to exposure is great, should be immunized. (2) It is of great value in differentiating between clinically doubtful cases of diphtheria, positive reactions being obtained in clinical cases, negative reactions in carriers. (3) It is useful in experimental work in determining the effects of various forms of immunization and the duration of immunity conferred by these methods. (4) It has a definite value in the handling of diphtheria epidemics in institutions. Kolmer and Moshage (*Amer. Jour. Dis. Child.*, March, 1915) studied "The Schick Toxin Reaction for Immunity in Diphtheria," and summarize their observations as follows: (1) The toxin skin reaction is a valuable and reliable method for detecting susceptibility to diphtheria. (2) Persons reacting negatively to this test usually contain at least $\frac{1}{20}$ unit of diphtheria antitoxin per cubic centimeter of serum, and this amount of antitoxin is probably sufficient to protect against infection. (3) Persons reacting weakly or strongly positive usually contain less than $\frac{1}{40}$ of a unit of antitoxin per cubic centimeter of serum or none at all. These persons may be regarded as susceptible to diphtheria and in the event of exposure to infection should be passively immunized with an injection of antitoxin. (4) About 40 or 50 per cent. of children, ranging from one to fifteen years of age, react positively to the toxin test; this means that the preliminary use of the toxin test will eliminate the necessity of administering prophylactic doses of antitoxin to about 50 per cent. of children. (5) The toxin reaction indicates that the immunity conferred by an injection of antitoxin begins to disappear after ten days and has generally passed away entirely after four weeks. (6) The increased susceptibility of persons with scarlet fever to diphtheria is shown by the toxin reaction; even after the injection of antitoxin about 10 per cent. are susceptible within ten days. (7) According to the toxin reaction the immunity conferred by an attack of diphtheria is usually of short duration or entirely absent. (8) The most practical application of the toxin reaction consists in applying the test as a preliminary measure to all persons who have been exposed to diphtheria and immunizing only those who react positively.

Pellagra.—The Thompson-McFadden Pellagra Commission of the New York Post-Graduate Medical School and Hospital has just issued its second progress report, in which it presents data confirming the previous impression that the disease is communicable and in some way associated with insanitary methods of sewerage disposal. These conclusions are directly opposed to those of Goldberger, of the Public Health Service, whose studies led him to believe that pellagra is due to a faulty dietary. The conclusions of the Thompson-McFadden Pellagra Commission, consisting of J. F. Siler, P. E. Garrison and W. J. MacNeal, are as follows: (1) The large active foci of pellagra in Spartansburg County were found in and near the large centres of population, and particularly in the cotton-mill villages. (2) Children under the age of two, adolescents for about five years following puberty, and adult males in the active period of life were least frequently affected by pellagra. On the other hand, women from twenty to forty-four years of age, old persons of both sexes, and children from two to ten years of age were most frequently affected. (3) No definite connection between occupation and the occurrence of pellagra has been found, although the high pellagra morbidity in the women and children points to the home as the place in which the disease is usually contracted. (4) In the group of incident cases most thoroughly studied, evidence of close association with a preëxisting case was disclosed in more than 80 per cent. (5) A house-to-house canvass of the homes of over 5000 people living in six endemic foci of pellagra failed to disclose any definite relation of the disease to any element of the dietary. (6) In these six villages new cases of pellagra originated almost exclusively in a house in which a preéxisting pellagrin was living, or next door to such a house, suggesting that the disease has spread from old cases as centres. (7) So far as we have observed, pellagra has spread most rapidly in districts where insanitary methods of sewage disposal have been in use. (8) Additional evidence has been obtained to support the conclusion that flies of the genus *Simulium* have nothing to do with pellagra. (9) Animal inoculations and the experimental study of intestinal bacteria have not yielded conclusive results. (10) The studies of the blood have shown a lymphocytosis in most cases, but have not disclosed any constant abnormality characteristic of pellagra. (11) There is no evidence of inheritance of pellagra. (12) The immediate results of hygienic and dietetic treatment in adults have been good, but after returning to former conditions of environment, most of the cases have recurred. In children, prognosis is very much more favorable.

Geographic Distribution of Plague and Its Menace to the United States.—W. C. Rucker (*Public Health Reports*, May 14, 1915, p. 1428), in his article, recites the distribution of bubonic plague throughout the world with special reference to the lines of travel from such localities to the various borders of the United States. The measures to be adopted for the prevention of the introduction of plague into the United States are considered under four general headings. The first of these is the maritime quarantine, which the author states can be absolutely effective only at the cost of great interference with commerce. The second line of defense is at the wharves and consists in the prevention of embarkation or disembarkation of rodents; but this is a measure on which absolute reliance cannot be placed. The third line of defense consists in the immunization of human beings against bubonic plague; but this is at best a poor procedure and, in the absence of an epidemic, is manifestly impracticable. The fourth line of defense consists in rat-proofing the environment in which man works and lives. All other methods of prevention may be used; but the one on which the greatest reliance can be placed, and from which lasting protection may be obtained, is by the insulation of man from the animal which serves as the disseminator of bubonic plague. Any city which will render itself completely rat-proof need have no fear whatever of the disease. The eradication of plague from the city of New Orleans has already cost the Federal, State, and municipal governments upward of $400,000, exclusive of the large sums which corporations and private individuals have expended in rat-proofing. This amount of money would have gone a long way toward building permanent fortifications against rats.

A Microscopic Test For Pasteurized Milk.—Frost (*Jour. Amer. Med. Assn.*, 1915, lxiv, 821) started to work upon the theory that it would be possible by means of an *intra vitam* stain to color live leukocytes. In this way the live cells in raw milk could then be distinguished from the dead cells in heated milk. Frost uses one part of a saturated aqueous solution of methylene blue to five parts of the milk to be tested. The dye should be added to the milk slowly to prevent the possibility of the stain coagulating the milk. The stain is left in contact with the milk for fifteen or twenty minutes, and the sediment of the stained milk is precipitated in a centrifuge and spread on a glass slide. When the smear is dry it is ready for examination. The entire microscopic field is stained a light blue in the case of raw milk. In this blue background appear numerous clear areas, the smaller ones being fat globules, the larger ones leukocytes. On the other hand, the smears made from heated milk do not have the background as deeply stained, and the leukocytes are always more deeply stained than the background. Only the polymorphonuclear leukocytes react in this way, for the mononuclear cells are always well stained.

The Germicidal Action of the Ultraviolet Ray.—Houghton and Lewis (*Amer. Jour. Pub. Health*, 1914, v, 225) conclude that: The ultraviolet rays produced by the Cooper-Hewitt mercury arc have a strong bacterial action. Certain species of bacteria in aqueous suspension, including spore-forming organisms, are killed by exposure to the rays. Molds, however, are only partially destroyed by the ultraviolet light. The action seems to be a photo-mechanical process, and is, in all probability, due to absorption of the ultraviolet rays by the bacterial protoplasm. Water, wines, many inorganic, and a number of organic substances in aqueous solution, can be sterilized by ultraviolet light. Bacterial vaccines require a prolonged action. Proteins and other bodies of high molecular weight interfere with the action of the rays. Turbidity, both organic and inorganic, has a similar action. Color, within certain limits, seems to have no influence.

Protective Inoculation Against Mumps.—A. F. Hess (*Proc. Soc. Exper. Biol. and Med.*, 1915, xii, 144) calls attention to the fact that mumps confers a marked immunity and that second attacks are rare. He therefore used the blood of convalescents as a prophylactic. Six to 8 c.c. was injected intramuscularly in 17 cases. These children were in wards where there had been cases of mumps for the past month and where it continued to appear for a month following these inoculations. In no case did one of the inoculated children develop mumps, whereas one-third to one-half of the non-inoculated cases developed the disease. The blood was taken from children who had just recovered or had been well for about ten days. It would seem that this proceeding could be made use of in the institution as well as in the home, and that this type of therapy could be adapted in the case of measles and other infectious diseases.

PATHOLOGY AND BACTERIOLOGY

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Hypertrophy of Right Heart Following Inflammatory Thickening of Pulmonary Arterioles.—Schutte (*Centralb. f. Path.*, 1914, xxv, 483) reports this finding in a woman aged seventy-four years, who died of cardiac insufficiency with generalized edema. The right ventricle was hypertrophied and dilated and formed the apex of the heart. The left heart with its valves was quite normal and the aorta with its branches was unusually free from sclerotic change. Macroscopically nothing was found to account for the hypertrophy and dilatation of the heart. The microscopical study of the lung, however, showed a thickening of the intima of the pulmonary arterioles of certain constant caliber. The vessels of only a particular size appeared with the intimal lesion and the condition was more marked in the left upper lobe than elsewhere. The intimal thickening was of an inflammatory and proliferative kind. No associated lesion was found to explain the localized inflammatory process of the arteries of the lungs.

The Localization of Emboli in the Lung.—Ribbert observed that emboli coming from the inferior vena cava usually localized in the lower lobe of the lung. This was substantiated by Kundrat who found that the emboli of puerperal sepsis passed to the lower lobes while those of otitic origin were found in the upper lobes. The animal experiments of Virchow, however, showed that foreign bodies introduced into the jugular vein of the dog were most commonly found in the lower lobes, while similar experiments by Behring with tubercle bacilli demonstrated the most usual lesion in the upper segments of the lung. Kretz in following human autopsy material came to the same conclusion as Ribbert and his pupil Helly substantiated these results in a series of animal experiments. It would appear from these findings that there are definite currents within the blood mass of the heart and large veins. In fact, Kretz has suggested a theory of these currents by which the blood of the upper cava passes to the upper pulmonary artery and from here goes through the heart in such a manner that it is driven into the aorta and to the lower portion of the body. The blood returning from these parts by the inferior cava is driven to the lower pulmonary system and upon its return to the left heart passes to the aorta so that it reaches the vessels of the upper extremities and head. These rather far-fetched theories have not been substantiated by others. ALWENS and FRICK (*Frank. Ztschr. f. Path.*, 1914, xv, 315) carried out animal experiments in which they injected bismuth suspensions into the ear or femoral veins. The lungs were examined during life and after death with the Roentgen-ray. By this means they were able to observe the course of the injected materials quite accurately. Besides this, histological examination of the specimens was also undertaken. They were unable to agree with the Kretz findings and could offer no evidence that the blood from the upper and lower portions of the body remained in separate streams. In the living animal they could observe that the blood in the ventricles was fully mixed. They found, however, that the injection of larger quantities of foreign material led to the localization of much of it in the lower lobes of the lung. This localization occurred in this tissue regardless whether it was introduced into the jugular or femoral veins.

Variability of Pathogenic Bacteria.—Bacteriologists have long been interested in the variations developing among pathogenic bacteria. BERNHARDT (*Ztschr. f. Hyg. u. Infectionskrankh.*, 1914, lxxix, 179) has contributed to the subject some important results. He worked chiefly with strains of B. typhosus, and the diphtheria group but also records observations on B. paratyphosus, meningococcus, the bacillus of fowl cholera and the bacillus of rabbit septicemia. The alterations he obtained with the B. typhosus were marked changes in the types of colonies, cultural differences in broth, variations in agglutination, and loss of motility. In his series of experiments he was able to trace all degrees of variations from the original strains to the extreme variants. He also found marked differences in the permanency of these variations. One variant of B. typhosus lost its motility and remained non-motile during the period of observation, one and a quarter years, even after animal passage or frequent transfers. He was unable to find any fundamental differences in agglutination or antigen powers in the altered strains. Most of his variants were obtained from broth cultures at different periods of growth and he found that variants tended to disappear and that types closely resembling the original remained in the older cultures. Among the members of the diphtheria group the principal changes obtained were in morphology, colony formation and toxin production. All graduations in variation were noted. These alterations were mostly from broth, Loeffler's serum and agar, but he also obtained alterations by animal passage. The author believes that the changes obtained upon media also take place in man and supports his view by the finding of atypical forms in the nasal cavity and the urine of diphtheria patients. In two cases, both fatal, he grew true diphtheria bacilli from the urine. Some of his alterations were accompanied by lowered resistance and in others by increased viability. The latter was especially observed in the altered types of the bacillus of rabbit septicemia and meningococcus. The author discusses very fully the theoretical and practical significance of his findings and those of others. He believes that the source of these alterations is to be found chiefly in the metabolic products of the bacteria and that different bacteria react differently to the various stimuli. Moreover, he does not agree with the view that the bacteria are predisposed by these means and that sudden changes take place. It is a gradual alteration. He also shows that the variations are not necessarily of any benefit to the bacteria but take place irregularly and almost by chance. An attempt is made to correlate these findings with the general problem of heredity and he discusses the use of such terms as mutation, modification and variety and points out that they can only be used in a relative sense.

The Widespread Distribution of Diphtheroids and Their Occurrence in Various Lesions of Human Tissues.—Considerable confusion has been brought to the minds of many investigators by the finding of diphtheroid organisms in a great variety of human tissues. At times, an important relation is suggested between the organism and the diseased tissue; as in Hodgkin's disease and leprosy. Much difficulty is also experienced in designating the limits of the group. In one direction they advance closely to the true diphtheria bacillus, while in the other, transition forms closely approach the streptothrix group. Harris and Wade (*Jour. Exper. Med.*, 1915, xxi, 493) have pointed out the wide distribution of this group of organisms in the human body. Under normal conditions it has been shown to be present in the eye, brain and cerebrospinal fluid and blood cultures. The authors have obtained them from lymph glands in simple hyperplasia while others have laid much stress upon the importance of finding the diphteroids in the lymphatic system. Moreover, similar organisms were obtained from benign and malignant tumors of various kinds, but in no instance could any etiological importance be laid to them. Diphtheroid forms are also not uncommon upon the skin and in the air. The various diphtheroid organisms which have been isolated may to a certain extent be differentiated but up to the present no accurate precedure has been developed, whereby a suitable classification may be employed.

On the Mechanism of Pneumococcus Immunity.—Boehncke and Mouriz-Riesgo (*Ztschr. f. Hyg. u. Infectionskrankh.*, 1915, lxxix, 355) believe that the promotion of phagocytosis is a more important function of pneumococcus sera than the antitoxic activity. From the experiments these authors, along with other investigators, have shown that pneumococcus sera possess a very definite antitoxic principle but that the animals are not cured by its use. The time of death is, however, definitely delayed. These sera promote phagocytosis and by this means exhibit their most important function in curing cases of pneumococcus infection.

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ORIGINAL ARTICLES

ROENTGEN DIAGNOSIS OF GASTRIC CANCER: REPORT OF TWELVE CASES.

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In the detection of cancer of the stomach, the Roentgen rays take precedence over all other methods, despite the fact that "we are only in the daguerreotype stage of Roentgen-ray photography."[1] In the Mayo Clinic, 95 per cent. of gastric carcinomas are discovered by this means, a percentage which is not approached by any other process of examination.

Since nearly one-third of all cancers occur in the stomach, and since early recognition and operation alone afford a chance of cure, any measure which will increase the number of correct and early diagnoses is of the highest importance.

Prior to the development of gastric roentgenology, diagnostic reliance had to be placed upon the history, the physical examination and the gastric analysis. Significant in the history were: middle or advanced age of the patient; digestive disturbance, such as anorexia, vomiting, occasionally pain, hematemesis, etc.; cachexia and loss of weight. By the physical examination the presence of a tumor was sought for. The gastric analysis was scanned for achlorhydria, food remnants, blood, and Oppler-Boas' bacilli.

It is quite clear that the most important of these evidences can result only from a cancer which is well advanced or one which is obstructive. The records of our Clinic show that in a large series of cases confirmed by operation, 67 per cent. of the patients had palpable tumors and 53.3 per cent. had food remnants. In other words, 33 per cent. had no palpable tumors and 46.7 per cent. had no food remnants to indicate obstruction. It is precisely in those cases which show neither tumor nor food remnants that the Roentgen-rays have their greatest field of usefulness and superiority. It is no longer necessary to wait until the tumor is palpable or until evidences of marked obstruction exist.

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[1] Mayo, W. J., The Cancer Problem, Journal-Lancet, 1915, xxxv.

There is no intent to say that the clinical data should be discarded. On the contrary, the roentgenologist should in every instance be acquainted with the clinical facts. If suggestive of cancer, they will stimulate him to a more exhaustive search. If negative, they will exercise a wholesome restraint upon his interpretation of the reflex phenomena so often produced by conditions outside the stomach. More important still, the final diagnosis should be compatible with all the findings, if possible, and occasionally only their correlation will make the diagnosis. A combination of all methods forms a net through which few cancers will escape.

It must be conceded that the carcinomatous character of tissue can be positively determined only by the microscope, and the Roentgen rays can merely show the presence of a gastric tumor, which may or may not be malignant. However, benign gastric neoplasms are uncommon; according to Graham,[2] 95 per cent. of tumors of the stomach are cancer. Further, in the occasional instance of a non-malignant new growth, if the salient features of the clinical history are considered, the diagnostician will be at least suspicious of the fact.

The roentgenologic manifestations of gastric cancer include departures from the normal contour, pyloric action, peristalsis, motility, flexibility, mobility, position, and size of the stomach. Enumerated in the order of their relative importance, these signs are:

1. Filling defects.
2. Alterations of pyloric function: (*a*) gaping of the pylorus, (*b*) obstruction of the pylorus.
3. Perversion of peristalsis: (*a*) absence of peristalsis from involved areas, (*b*) weak peristalsis, (*c*) antiperistalsis, (*d*) exaggerated peristalsis, (*e*) irregular peristalsis.
4. Altered motility: (*a*) rapid and early emptying (non-obstructive cases), (*b*) delayed empyting (obstructive cases).
5. Lessened flexibility.
6. Lessened mobility.
7. Diminished size (capacity).
8. Displacement.

Filling Defects. The filling defect is the basic radiologic sign of cancer and practically indispensable to a positive diagnosis. It is occasioned by the projection of the tumor into the barium-filled lumen of the stomach, thus producing irregularity of contour. At the stage at which most patients first come for examination, the tumor usually has attained considerable size, and the filling defect is sufficiently extensive to be readily seen.

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[2] Differential Diagnosis of Diseases Causing Gastric Disturbance, Northwestern Lancet, 1910.

In aspect, filling defects vary somewhat according to the character and seat of the neoplasm. The fungoid cancer often shows multiple gross irregularities, gradually shading off into the barium shadow, giving a more or less stereoscopic effect to the elevations and depressions.

The infiltrating scirrhous cancer may greatly, though somewhat irregularly, narrow the lumen of the affected portion, which is most commonly the pyloric end.

A small cancer at the pylorus may produce a broadening of the duodenopyloric hiatus or a conical vestibule. A more extensive cancer may seemingly cut off the entire prepyloric segment.

Cancer of the pars media may result in an hour-glass deformity. High up in the cardia the tumor may infringe upon the contour of the gas-bubble and contrast with the translucency of the latter.

A tumor on the anterior or posterior wall alters the contour in the sagittal view; in the anteroposterior view it may show centrally as a less dense area within the barium shadow.

The actuality and permanence of filling defects cannot be determined with finality by a few roentgenograms alone. Essential here is the screen examination, during which the gastric shadow can be studied at various angles by turning the patient and the effect of active and passive movements observed.

A true filling defect is permanent, showing no change in location or appearance after palpating manipulation, after administration of antispasmodics, or upon reëxamination.

Absence of peristalsis from the suspected area is highly confirmatory.

The correspondence of a filling defect to a palpable mass is strongly indicative of its genuineness.

Irregularity of outline and lack of symmetry are rather constant in true filling defects.

Filling defects in the pars media are less likely to be overlooked than those in the pars cardiaca or the pars pylorica. A filling defect high up in the cardia may not contrast strongly with the translucent gas-bubble. It may be brought into better relief by pressing the barium upward, or by screening and plating in the recumbent position. Small, filling defects in the pars pylorica require careful study for detection, owing to the difficulty of obtaining a clear outline of this region, because of its proximity to the spine, and the tendency of the barium to settle away from the pylorus of a fish-hook stomach. A small defect, which may be well seen in the partly filled stomach, may be concealed in the distended stomach. Hence, observation should be made during the process of ingestion as well as after repletion. The screen diaphragm should be actively employed and the aperture narrowed to increase the distinctness of small suspected areas, thus facilitating close scrutiny. Filling defects situated in the pars media often produce hour-glass deformity. More commonly such an hour-glass is of the X-type in contradistinction to the usual B-type of gastric ulcer or spasm, but this distinction is not invariable. As a rule, the hour-glass of cancer lacks the sharply defined contour of the hour-glass due to ulcer or spasm, and shows an indefinite shading off.

Filling Defects from Causes Other than Cancer. Filling defects, either apparent or real, may be produced by numerous conditions other than cancer. Apparent filling defects may result from the use of faulty media (stiff media, poorly mixed or without sufficient barium; secretion in the stomach; food remnants; hair ball (trichobezoar); gas or fecal matter in the colon; barium in the bowel adjacent to the stomach; lordosis and scoliosis; pressure of the stomach against the spine; pressure of a deformed costal arch; strong retraction of the upper abdominal wall; spasm; adhesion from perigastric inflammations; extrinsic tumors, including those of the liver, spleen, pancreas, kidney, large and small bowel, omentum, mesentery and belly wall; displacement and distortion of the stomach by ascites, ovarian cysts, pregnancy, etc. Actual filling defects not distinguishable of themselves from those of cancer, may be caused by various benign tumor-producing lesions of the stomach.

Faulty media in which the barium is irregularly distributed may give varying degrees of opacity in the gastric shadow and thus imitate filling defects. The mixture may be too stiff, poorly mixed, or an insufficient quantity of barium may be used. With very thin mixtures the barium often settles to the lower pole, leaving irregular shadings along the lesser curvature. A little palpatory shifting of the gastric contents readily shows the character of these pseudodefects, and erroneous interpretation is not likely to occur unless an attempt is made to base a diagnosis upon plates alone.

An excessive amount of secretion in the stomach, while it usually rises above the opaque meal, may mingle with it irregularly or thin its consistence. Sometimes secretion is imprisoned in the pyloric end of a fish-hook stomach, showing as a clear area above the opaque meal. The straight horizontal line of demarcation between the secretion and the barium is indicative of the artificial nature of the defect. By palpatory pressure the secretion can be displaced by the meal, or is passed into the duodenum.

Food masses in the stomach, by excluding the barium from the area in which they lie, may simulate filling defects. Here palpatory shifting of the gastric contents will cause the seeming defect to change its situation or disappear. However, as a matter of routine, patients should be examined only in the fasting condition. Employment of the tube to withdraw food remnants in cases of pyloric stenosis, unless otherwise contra-indicated, may be resorted to if desirable.

Occasionally a hair ball (trichobezoar) is found in the stomachs of neurotic persons who are addicted to biting the hair. The accumulation may be a rounded ball of various size, or may form a complete cast of the gastric cavity. After giving the barium meal, the stomach shows an area of diminished density somewhat like the filling defect produced by cancer on the anterior or posterior wall, the peripheral contour showing fairly well. If the ball is small it can be displaced by manipulation or even forced up into the gas-bubble.

Gas in the colon is a common source of annoyance. Even after preparation of the patient by purging there is usually more or less gas in the splenic flexure. Frequently the distention is sufficient to infringe upon the greater curvature and produce considerable irregularity. Such irregularities ought not to be very deceptive, as they change with manipulation, and the distention of the transparent loop of intestine is rather obvious. If the gas-bubble is intruded upon, the colonic haustra are usually evident. Occasionally the transverse colon may be displaced upward and lie directly across the stomach. Its course may be traced by its transparency and haustration. Fecal matter in the bowel might possibly cause indentations in the adjacent gastric contour, although we have never seen this condition.

Masses of barium from the six-hour meal, in the bowel adjacent to the stomach, sometimes produce apparent irregularities of the gastric contour on the plate. By the screen examination with changing positions and palpation their character is easily seen.

Deformities of the dorsal and lumbar spine, including lordosis and scoliosis, may deform the contiguous gastric contour. Such conditions are rather manifest and rare.

Pressure of the stomach against the spine, either normal or with well-marked physiological lordosis, often disfigures the transspinal portion of the stomach. This disfigurement is often seen on the plates made with the patient's abdomen pressed tightly against the cassette. Not rarely it is also observed during fluoroscopy, especially when the patient maintains a high degree of abdominal rigidity and tension.

Strong retraction of the belly wall sometimes occasions a wide, regularly curved depression in the greater curvature of the stomach just below the left costal arch. Its smooth, sharp outline and its situation should differentiate it from an actual filling defect.

Spasm of the gastric musculature may produce very deceptive imitations of the filling defects caused by cancer. Migrating or intermittent spastic contractions, which are frequently seen, are evidently spasmodic because of their changing situation or interruption; but spasm is not always migratory or intermittent. Often a non-moving, spastic incisura will indent the stomach so as to form an hour-glass, exactly simulating an organic hour-glass stomach. In other cases the entire pyloric portion of the stomach may be constricted to a stiff, narrow tube, rolling under the palpating fingers as a cylindrical mass. Again, the entire stomach may be spastically contracted, small, and of finely irregular contour, without definite peristalsis. In all the above conditions the outline of the stomach, though not regular, is sharply defined, and this circumstance should put the observer on guard. However, there is still another variety of spasm which is dangerously misleading; in this form the barium shadow in the spastic area, which may be large or small, fades off toward the gastric periphery, exactly as though intruded upon by a tumor mass. The spasm may sometimes be effaced by massage during the screen examination, but reappears, as a rule. If accessible to palpation the absence of a tumor from the suspected region should suggest cautious interpretation. The pyloric portion of the stomach is a common seat of this spastic deformity.

The points of difference between the true filling defects and those produced by spasm can be summed up as follows:

The true defect is permanent, often corresponds to a palpable mass if accessible, and is not often sharply delineated.

The spastic filling defect is often migratory or transient, is frequently sharp in outline, and the contracted muscle is rarely palpable. Spasm may disappear upon distracting the attention of the nervous patient or by causing him to relax his abdomen, or by vigorous palpatory manipulation; or it may disappear or change its situation at a second examination. In a great many cases reëxamination after the administration of an antispasmodic is necessary. Belladonna, atropin, and papaverin are the drugs most generally employed. Commonly we give the tincture of belladonna in 15 ♏ doses, t. i. d., for two or three days or until the patient shows its effects. This procedure should never be omitted in any case in which the possible existence of spasm cannot absolutely be eliminated. In rare instances spasm may persist in spite of this measure, but such cases are quite uncommon.

Adhesions from perigastric inflammations may produce distortions and irregularities resembling the filling defects of cancer. The inflammatory process originates most commonly from perforating gastric ulcer or from pericholecystitis. A perforating gastric ulcer in the pars media producing perigastric adhesion is apt to reveal its identity by a pocket, a niche, or an incisura. Perforating ulcer in the pars pylorica may be less characteristic, but these cases have been quite rare in our experience.

Pericholecystitis, with extensive adhesions about the pars pylorica, accompanied, as it often is, by a gaping pylorus and sometimes producing a palpable mass, may be difficult to differentiate from cancer. Here only careful judgment of all the facts will prevent diagnostic error.

Tumors extrinsic to the stomach may deform its contour. Such tumors may originate in the liver, spleen, pancreas, kidney, large or small bowel, omentum, mesentery, or belly wall. As a rule, the filling defect occasioned by their thrust into the gastric lumen is quite smoothly regular, the inequalities of the tumor being covered by the wall of the stomach. Unless adherent to the stomach, which is not usual, changes of position of the stomach with respiration or by palpation will alter the location of the filling defect. In these cases, also, the peristalsis is usually normal, and this fact speaks against a tumor of the stomach itself.

The stomach may be eccentrically distorted and displaced by ascites, ovarian cysts, and other large abdominal tumors, pregnancy, or even by a tensely retracted abdominal wall. Such conditions should be rather patent.

Intrinsic tumor masses produced by syphilis and benign neoplasms, as well as varicosities of the gastric veins, may cause filling defects practically identical with cancer. These conditions are so unusual that the roentgenologist should not be unduly alert for them.

Alteration of Pyloric Function. In cancer the pyloric function may be perverted in either one of two quite opposite ways: namely, either by gaping or obstruction. The barium water often flows through a normal pylorus, with little or no interruption; but as soon as the thicker pap is given the flow usually becomes scanty or intermittent. The gaping pylorus of cancer is characterized by a free and continuous exit of both mixtures into the intestine. Very commonly the stream is voluminous and the upper small bowel is speedily filled with the opaque mixture. The stomach may be almost or even completely emptied during the brief period of examination.

Gaping of the pylorus results from an interference with its sphincteric contraction, either by infiltration and stiffening of the muscular ring or by an absence of the pylorus-closing reflex. Thus it is seen quite typically in scirrhous cancer involving the pars pylorica, but it is also found in association with cancers of the cardia or media, either scirrhous or medullary. A free and continuous flow somewhat similar to that seen with the gaping pylorus of cancer may be found in other conditions, such as duodenal ulcer, gall-bladder disease (with or without adhesions), achylia, certain diarrheas, and sometimes even in chronic appendicitis. It should be said, however, that in these conditions the flow is less voluminous, as a rule, than that noted typically in cancer.

Pyloric obstruction, as evidenced by a six-hour residue in the stomach occurs in about 60 per cent. of gastric cancers—oftener than with any other lesion. The amount of residue varies with the degree of obstruction. In the majority of instances cancers producing pyloric obstruction are of the medullary type. It is noteworthy that the lumen of the pyloric canal may be considerably diminished by the intrusion of a cancer without resulting in a six-hour residue, for the reason that the lessened caliber is compensated by the lack of sphincteric control. Since numerous causes other than cancer may operate to produce a six-hour gastric retention, the presence of a residue should not be given undue weight in making the final diagnosis, but its occurrence should stimulate a careful search for filling defects and other evidences of cancer.

Peristalsis. The perversions of peristalsis resulting from gastric cancer are varied. Absence of peristalsis from a cancerous area of the gastric wall due to local loss of muscular contractility is a highly valuable sign. In some such instances a wave may progress to the affected site, skip it, and take up its course again beyond, and this observation is one test for the genuineness of cancerous filling defects. Weak peristalsis, the waves being both shallow and infrequent, is fairly common in cancer. Frequently the stomach seems to be perfectly inert. Antiperistalsis is occasionally observed in cancer with pyloric obstruction. The antiperistaltic waves are best seen on the greater curvature in the pars pylorica and media. The waves are usually wide and shallow, though sometimes deep. Beginning at the pylorus, they sweep slowly backward and disappear in the upper media. They may coexist with peristaltic waves traveling in the normal direction. Exaggerated peristalsis, as a sequence of cancer with pyloric obstruction, is more rare than might reasonably be supposed. When seen, the exaggeration is usually more marked on the greater curvature. Peristalsis in cancer may show other eccentricities. It may be irregular as to the depth and succession of the waves; a fairly deep wave may be closely followed by a shallow one, while the next may be normal as to depth and rhythm. None of the foregoing perversions of peristalsis is peculiar to cancer, and they are merely indicative of a pathological process.

Altered Motility. Emptying of the cancerous stomach may be either retarded or accelerated, according to the presence or absence of pyloric obstruction. In the non-obstructive cases hypermotility is the rule, and is a natural sequence of the achylia and gaping pylorus. The acceleration of gastric clearness may be extreme and the stomach evacuate itself with extraordinary rapidity. The acceleration is often exhibited not only in a rapid and early clearance of the stomach, but also in an advanced position of the six-hour meal, the head of the barium column appearing in the transverse colon, the splenic flexure, the descending colon, or even the ampulla. In the obstructive cases, delayed clearance is shown by the six-hour residue. That portion of the meal which has passed through into the intestine may or may not show retarded progress. It is to be remembered that gastric motility may be affected by many things other than cancer. Hypermotility of moderate degree is a common sequence of non-obstructive duodenal ulcer, achylia, and diarrheic conditions. Hypomotility, with or without a six-hour retention, may result from any sort of organic obstruction at the pylorus or near beyond, or from reflex pylorospasm.

Lessened Mobility. By involving adjacent structures a cancer not infrequently produces more or less fixation of the stomach. The attachment may be to the abdominal wall, or to the liver, pancreas, or other viscera. The presence of fixation may sometimes, but not always, be determined by palpatory maneuvers, depending upon the position of the stomach, the situation of the attachment, and the degree of laxity of the abdominal wall, and, also, by observation during forced respiration. The small, high-lying, contracted stomach, inaccessible to manipulation, though it appears to be fixed, is not necessarily so. On the other hand, a stomach which has a free and flexible lower pole may seem to be freely mobile, when there are definite adhesions on the lesser curvature. Inasmuch as fixation is simply an indication of extragastric involvement, it is merely a contributory sign of cancer. It may be taken into account in estimating the possibility of resection.

Lessened Flexibility. Diminished flexibility of the cancerous gastric wall is a practicable and valuable sign, especially of scirrhous cancer. Upon narrow palpation with a single finger or with the ulnar edge of the hand the accessible normal gastric wall will show corresponding indentation, whereas if stiffened by infiltration it will either be disproportionately indented or be moved aside *en masse*. The loss of pliability may also be somewhat evident by the lack of contour change during deep respiration or during variations of abdominal tension. Further, it may show as a lack of expansibility in the affected portion during the process of filling the stomach, the lumen of the involved area being almost constant in size at all degrees of repletion, while the unaffected portion expands to accommodate the increased volume.

Diminished Size and Capacity. A common feature of the cancerous stomach is marked diminution of the capacity and apparent size. The reduction may be the result either of the projection of large fungoid masses into its lumen or the shrinking effect of scirrhous infiltration. In extreme instances, the effort to accommodate the ingesta causes a backing up of the meal in the esophagus, which latter may show dilatation. Besides cancer, other causes which may lessen the capacity of the stomach are perforating ulcer, with extensive perigastritis, spasm, and benign lesions. The upper loculus of an hour-glass stomach may be mistaken for a contracted stomach if the presence of the lower loculus be overlooked. It must also be remembered, on the other hand, that an obstructive cancer at the pyloric end may result in considerable dilatation of the stomach. A similar dilatation may be consequent upon other obstructive causes. It follows then that neither large nor small size of the stomach is especially significant of cancer, but marked variation in size of the stomach is at least suggestive of the presence of a lesion.

Displacement. The predilection of cancer for the pyloric end of the stomach, often with more or less complete obliteration of the distal portion of its lumen, results frequently in an apparent displacement of the stomach to the left, since its proximal portion only is visualized. Aside from this, however, there may be actual displacement upward and to the left in cases of scirrhous cancer, and the diminished organ may lie entirely up under the shelter of the left costal arch. Somewhat similar displacements may occur as a result of perforating ulcer, ascites, tumors outside the stomach, and retraction of the abdominal wall.

PATHOLOGY. With the microscopic pathology of gastric cancer the roentgenologist has little concern, but the roentgenologic appearances of cancer sometimes depend quite considerably upon its character as affecting its form, location, and extent. Hence, a few statements concerning certain anatomical varieties of cancers and their gross aspects may assist in clarifying the description of this lesion, as seen by the Roentgen rays.

Cancers of the stomach invariably originate in the mucous layer. While they are all basically epithelial neoplasms, they present numerous structural differences. Disregarding those variations which are here unimportant, there are three forms which are of chief interest from a radiologic standpoint:

1. A proliferative form, almost wholly epithelioid in composition, with circumscribed tumor production. This is the *fungous* type with which may be included for present convenience the medullary (encephaloid), cauliflower and adenocarcinomas. It is characterized by a relatively small amount of interstitial tissue, and hence is soft.

2. An infiltrative form. This is the *scirrhous* type. Speaking in a general way, it infiltrates the gastric wall with less irregularity and less projection into the cavity of the stomach than is seen in the fungous type. It is characterized by a relatively large amount of interstitial tissue, is hard, and is more frequently associated with ulceration than the other types. The infiltration may be either (*a*) localized or (*b*) general.

(*a*) When localized, the pyloric end of the stomach or the lesser curvature is the part most commonly affected, the greater curvature being rarely involved at the beginning.

(*b*) The general diffuse infiltration involves a large part or the whole of the stomach, which is thick-walled and contracted. This is regarded by many as identical with the so-called "leather-bottle" stomach, or "diffuse fibrosis," and is rather rarely seen.

3. A degenerative form, the so-called "colloid," or, more correctly, mucoid cancer. In this form the cells lose their structure and become merged into a homogeneous mucoid mass. Mucoid degeneration may occur in either the fungous or scirrhous type.

It will be understood that the three forms mentioned do not always or necessarily exist independently of each other, that the classification and descriptions are practical rather than accurate, and that differentiation of these forms is not always easy. Sometimes these pathological differences in gastric cancers are sufficiently manifest in the roentgenologic picture to warrant an opinion as to their probable nature; however, such an opinion should be advanced with caution, and then only in those rather few cases which are typical, for, in the majority of cases, the roentgenologist would better be content with a diagnosis of cancer without attempting to specify the particular variety.

Roentgen Characteristics of Fungous Cancer. In a broad way the typical fungous (medullary, encephaloid) cancer shows the following:

1. A non-shrinking effect upon the stomach as a whole. While the capacity of the stomach may be somewhat lessened by the encroachment of the mass upon its lumen, the gastric dimensions are not otherwise diminished. Often the hook form is preserved and this retention of the hook form has been suggested by Haudek as an indication of resectability.

2. Occasional involvement of the greater curvature, especially of the body of the stomach.

3. Sharp delimitation of the involved from the non-involved portion of the gastric wall.

4. Often large, multiple, irregular filling defects projecting into the gastric lumen and shading gradually into the central barium shadow, somewhat resembling impressions upon paraffin.

5. If at the pyloric end this type is likely to produce obstruction.

Roentgen Characteristics of Scirrhous Cancer. Typical advanced scirrhous cancer may be recognized by:

1. Its marked shrinking effect upon the stomach. The capacity of the stomach is not merely lessened by a filling defect, but is greatly diminished by the loss of expansibility due to widespread infiltration as well as actual contraction.

2. Frequent involvement of the pyloric end and lesser curvature. Quite commonly a scirrhous completely encircles the pyloric end and the deformity thus produced gives the stomach some resemblance to a curved funnel or an Indian pipe. The barium projects into the canalized pyloric mass as a smooth or slightly irregular spicule.

3. Gradual merging of involved into non-involved portion of the gastric wall. The limits of the lesion are difficult or impossible to determine radiologically. The lesion is usually more extensive than the picture indicates.

4. The filling defects of scirrhous cancer are commonly less grossly irregular than those of the fungous type.

5. This type of cancer, even though involving the pars pylorica, is likely to show a gaping pylorus.

Mucoid Cancer. A markedly diminished, fairly regular central lumen surrounded by a thick-walled tumor mass is sometimes seen in extensive mucoid degeneration, but mucoid change can rarely even be surmised by the radiologic appearances. It gives practically the same screen and plate picture as the infiltrative form (scirrhous).

Carcinomatous Ulcer. While by far the greater number of gastric cancers manifest themselves frankly as tumors at the time the patients present themselves for examination, ulcers are found occasionally which show microscopic evidence of malignancy. In their gross characteristics and roentgenologic appearances these ulcers are not different from benign ulcers. In most instances the crater of the ulcer is visualized as a niche projecting from the gastric lumen. This may or may not be associated with hour-glass stomach, an incisura, or six-hour retention. The only suspicious feature sometimes shown by the Roentgen rays is the extraordinary large size of the ulcer crater. In a few of our own cases in which the niche was 3 or 4 cm. broad the ulcer was found on microscopic examination to be malignant.

OPERABILITY. In deciding the question of operation in a given case of cancer the Roentgen rays furnish information of high, often decisive, importance. Primarily, operability depends considerably upon the skill of the operating surgeon; but aside from this certain radiologic findings speak for or against operation, whether radical or palliative. The location, extent, and character of the cancer are all matters of fundamental weight. Growths involving the cardia or upper media are not accessible to resection, while those at the pyloric end or lower media are often resectable. Obviously, resectability depends also upon the extent of involvement, and this can be more nearly determined by the Roentgen rays than by any other method. The actual extent of a medullary cancer corresponds closely to that indicated radiologically. The limits of a scirrhous cancer are much less sharply defined in the Roentgen picture and a liberal allowance must be made in estimating the probable degree of involvement.

Free mobility of a cancerous stomach is an item favoring resectability, while marked fixation resulting from extension to adjacent structures makes successful intervention less probable. However, a cancer which does not extensively involve the stomach or appear to have lessened its mobility materially may at operation be found to have invaded and be adherent to a near-lying organ, such as the pancreas, and resection of the growth is impossible.

Retention of the hook form of the stomach, which has been advanced as an indication of resectability, is often found in cases that are manifestly inoperable.

Regarding metastasis, a factor which has always to be considered, the Roentgen examination can rarely give any knowledge. Extensive metastasis in the lungs may be observed casually during the screen examination, or an abnormally large shadow of the liver may be a suspicious circumstance and these should always be looked for; but widespread glandular metastasis may exist without detection.

Years ago, Czerny[3] pronounced cases of cancer with definite palpable tumors of the stomach to be inoperable. This is rather extravagant, since many such cancers are resectable, and when there is no glandular involvement or invasion of adjacent tissue the chance for cure is good. Further, not every palpable tumor is a cancer; the mass may be a perforating ulcer with adhesions, pancreatic cyst, floating spleen or various lesions originating in the gall-bladder.

On the clinical side, the evidences of inoperability have been summed up by Mayo[4] as follows:

"1. The cachectic patient with marked evidence of progressive gastric trouble which has lasted over a period of a number of months, with a fixed tumor lying to the left. Such a case would be clearly hopeless.

"2. It frequently happens that with cancer of any of the abdominal viscera there will be an escape of cancer cells into the peritoneal cavity. These will drop, by gravity, to the bottom of the pelvis and become attached often to the sigmoid. The "feel" of these various small metastases upon rectal examination is very characteristic. In women, not infrequently transplantation to the ovary occurs, setting up a secondary malignant cyst. The majority of cases of malignant adenocarcinomas of both ovaries have such origin, and women are sometimes unnecessarily submitted to operation for their removal.

"3. The supraclavicular fossa, especially the left side, should be examined for carcinomatous glands.

"4. Cancer cells free in the abdominal cavity can be carried by the lymphatics to the umbilicus, forming a distinct mass like a button. In doubtful cases I remove, under local anesthesia, a little portion of this "button umbilicus" for microscopic examination.

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[3] Quoted by M. B. Tinker, What Stomach Symptoms Justify Surgical Intervention? Jour. Amer. Med. Assn., 1915, lxiv, 1789.

[4] Cancer of the Stomach; its Surgical Cure, Surg., Gynec. and Obst., 1912, xiv, 115–119.

"5. Metastatic deposits, giving rise to nodular tumors in the liver or peritoneal cavity.

"6. Ascitic accumulations in the abdominal cavity, taken in connection with the history of the patient, have some value. It is necessary to eliminate other causes of ascites—for example, the heart, liver, kidneys, tuberculous peritonitis, etc."

Roentgenologic determination of the absence or presence of obstruction, its site and degree, aids materially in judging the advisability of palliative surgery and in selecting the operation, whether gastro-enterostomy, gastrostomy, or jejunostomy. In expressing any opinion as to operability, unless the cardia or upper media is definitely implicated, or unless the growth is extraordinarily extensive, the roentgenologist should be chary of saying that a case is inoperable, as he may thus deprive the patient of relief or cure at the hands of the surgeon. In the majority of instances exploration alone is the final word and the patient should be given the benefit of the doubt. Besides, there is always at least a remote chance that the most confident diagnosis may be wrong.

Early Cancer. The term "latent cancer" is sometimes applied to cancers which give rise to few or no symptoms or signs and which cannot be diagnosed clinically. Since "latent" also carries the sense of quiescence or dormancy, a condition which has not been proved as regards gastric cancer, the adjective "early" is perhaps preferable.

A very practical question is, "How early can the existence of a gastric cancer be determined by Roentgen rays?" Since even in advanced cases Roentgen rays show only the presence of an organic lesion, the nature of which can only be predicated upon all the circumstances of the case, the actual question is, "How early does gastric cancer reveal roentgenologic signs which may reasonably be attributed to cancer and consequently which justify surgical intervention?" Admitting that the only cure for cancer is early operation, early diagnosis is a matter of prime importance. Admitting also that there are no definite clinical findings in early cancer, the statement is warranted that next to the exploring finger of a trained surgeon, Roentgen rays will reveal more cancers in the early stages than will any other diagnostic means. Hence every patient of cancer age with indefinite gastric symptoms should be subjected to a Roentgen examination. But how early can cancer of the stomach be detected? That depends upon:

1. The character of the cancer, whether a frank tumor, an insidious infiltration or a cancerous ulcer.
2. Its situation.
3. The examiner's familiarity with the work.
4. The amount of roentgenologic evidence, together with the extent of clinical corroboration.

Cancer which begins candidly as a tumor projecting into the gastric lumen is susceptible of quite early recognition by reason of the filling defect which it produces. The test of this sign is its permanence, not its size, and we have been fortunate enough to find one which was not larger than a cherry. The discovery of even smaller ones is no doubt possible. A stealthy infiltrative cancer of the fibrous or scirrhous type may invade the gastric wall without producing a recognizable filling defect. In this event peristalsis should be notably absent from the involved area, and a local loss of flexibility may be evident upon palpation. When these signs alone exist they should be interpreted with caution; but in conjunction with a gaping pylorus, achylia and clinical indices, they may warrant a surgical exploration.

Carcinomatous ulcers for the most part show the same roentgenologic signs as simple ulcers. However, as stated, ulcers with excessively large craters are open to the suspicion of being cancerous.

The situation of a small cancer makes a decided difference in the chance of its demonstration. On either curvature of the pars media or pars pylorica, filling defects, even though small, can usually be visualized either on the screen or plate, or both; but such defects on the anterior or posterior wall might evade observation even in the oblique view. Trifling defects in the region of the gas-bubble are also apt to be overlooked. The percentage of cancers in the pars cardiaca is, however, small.

The experience of the examiner and his ability to see and interpret slight departures from the normal have some importance in the diagnosis of early cancers. The novice would better limit his diagnoses to those cases in which he can demonstrate a permanent filling defect, and which are at least suspicious clinically. Anyway, these features will be found in the vast majority of patients with gastric cancer who seek medical aid.

Patients with early cancer near the pyloric ring producing obstruction are more likely to come into the hands of the roentgenologist than patients with early cancer beginning elsewhere in the stomach. A six-hour retention, evidencing obstruction, may be the only abnormality of which the observer feels sure. In other cases there may be a slight but permanent irregularity of the prepyloric contour, with or without obstruction, in which one can only say with certainty that a lesion of some sort is present. While it is highly important that gastric cancers be discovered at the earliest possible moment, it is also highly important that the diagnosis shall be well founded, and where the Roentgen findings plus the clinical features of the case do not quite justify operative intervention, the patient should be reëxamined at short intervals until a decision is reached. The administration of belladonna to eliminate the possibility of spasm in doubtful cases is particularly advisable.

INTERPRETING THE SIGNS OF CANCER. The Roentgen indications of gastric cancer vary markedly in degree and in their combinations with each other, as will be seen in the case reports herewith appended. The cases with which the roentgenologist has to deal thus range all the way from those which are plainly cancer to those which are highly doubtful. Often he can only be positive that a pathological condition exists. In every case he should be acquainted with the salient clinical facts, which should at least grossly correspond to his own findings. If they do not agree, he ought to confirm his observations by repeated examinations.

Case I (97408).—Man, aged forty-three years. He had attacks of indigestion five years prior to examination, with slight pyrosis and vomiting, which ceased after medical treatment. For five weeks he has been having spells of sharp epigastric pain, relieved by rest and aggravated by exercise. No loss of weight. Hemoglobin 89. Total acids, 86; free HCl, 62; combined, 14; no food remnants. *Roentgen findings:* Small prepyloric filling defect. Retention of half the six-hour meal. Active peristalsis (Fig. 1). *Diagnosis:* Lesion at the pylorus. *Operation*: Resection four inches of stomach (Billroth, No. 1); early cancer on pyloric ulcer. *Pathologist's report:* Ulcer, early cancer.

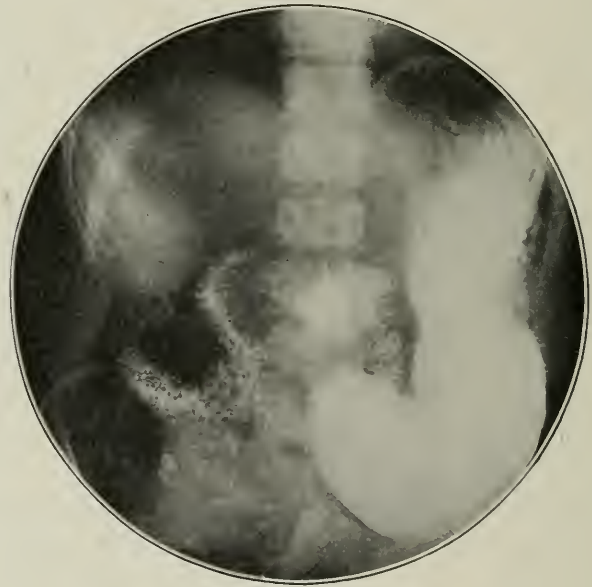

Fig. 1

It will be noted in the patient's history that the symptoms complained of were indefinite and not especially indicative of cancer. Such an early lesion could hardly have been discovered except by Roentgen rays or by exploration. This is a typical early case, in which good results can be expected from operation.

Case II (90713).—Man, aged sixty-seven years. Four months ago the symptoms began with belching and regurgitation of sour, foul-smelling water a half to one hour after meals. There was sticking, heavy, left epigastric pain soon after eating. Loss of weight 15 to 20 pounds. Total acids, 56; free HCl, 42; combined, 14; food remnants; blood. Epigastric resistance and tenderness, but no mass palpable. *Roentgen finding:* Small filling defect, pyloric end. No palpable mass corresponding to defect. Retention of three-fourths of the six-hour meal. Stomach large, showing irregular vigorous peristalsis (Figs. 2 and 2*A*). Fig. 2*A* shows the retention after six hours. *Diagnosis:* Carcinoma, pyloric end. *Operation:* Cancer in the pyloric end of stomach, ulcer type, with marked obstruction. Adherent to pancreas. Extensive glandular involvement. Resection of one-half of the stomach (Mikulicz-Hartmann-Billroth, No. 2). *Pathologist's report:* Cancer. Photographs of gross specimen shown in Fig. 2*B*.

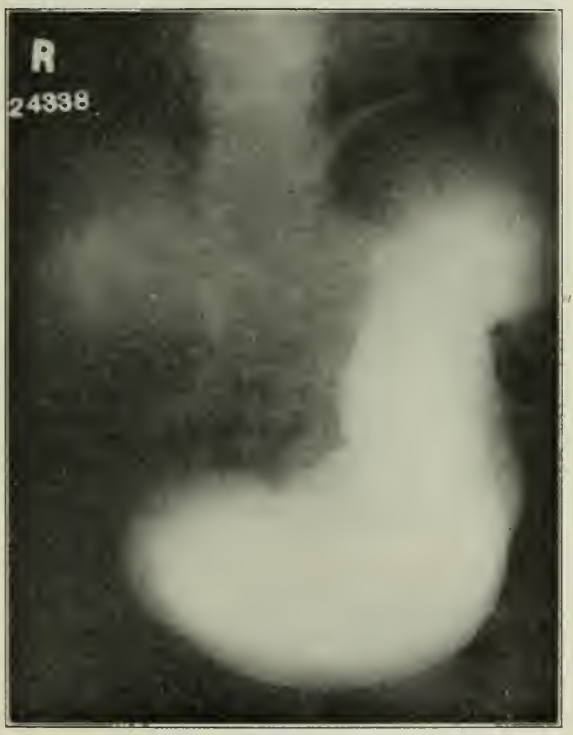

Fig. 2

While this is a fairly early case roentgenologically, as shown by the limited involvement of the stomach, the surgical findings prove that even small cancers of the stomach are not always favorable for resection, because of extension to adjacent tissues and glandular involvement.

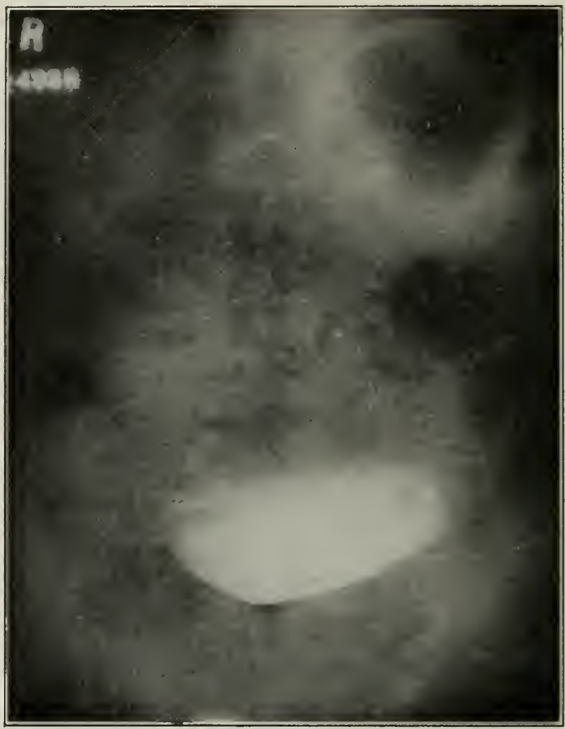

Fig. 2*A*

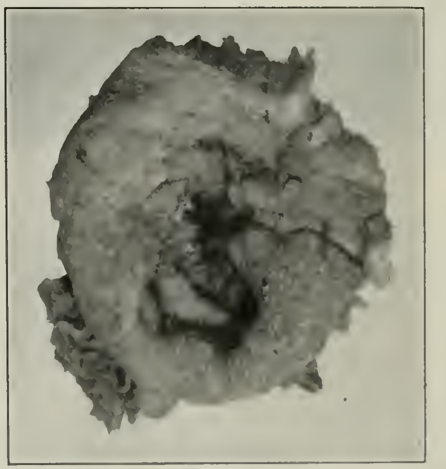

Fig. 2*B*

Case III (122965).—Man, aged thirty-six years. This patient had had indigestion off and on for ten years. Onset of present trouble two months ago. Distress, gas and nausea three or four hours p. c., with regurgitation of acid and mucus. Loss of weight 8 pounds. Movable ridge at right epigastrium. Total acids, 40; free HCl, 0; combined, 40; food remnants, 2; blood, yeasts, sarcines. *Roentgen findings:* Large stomach, containing three-fourths of the six-hour meal. Filling defect in the pars pylorica corresponding to a palpable mass (Fig. 3). *Diagnosis:* Cancer, operable so far as the extent of the involvement of the stomach is concerned. *Operation:* Resection of two-thirds of the stomach (Mikulicz-Hartmann-Polya). Cancer, pyloric end. *Pathologist's report:* Cancer with glandular involvement.

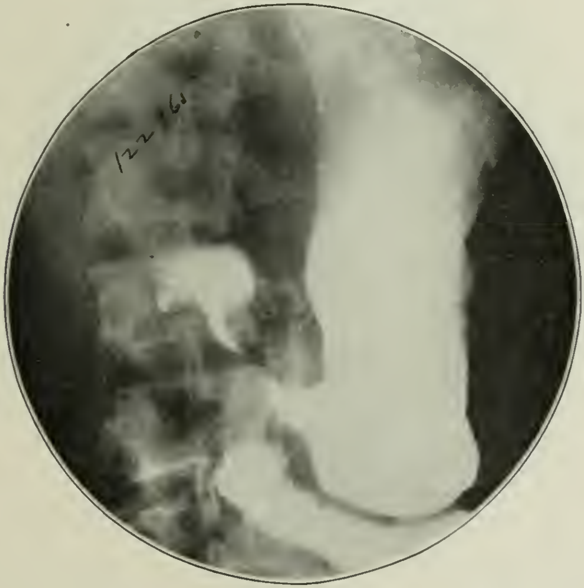

Fig. 3

This patient had slight gastric disturbance for ten years, as stated above, and had been seen repeatedly by competent gastro-enterologists, one of whom sent him to Europe for a vacation trip. Another sent him to Florida last winter. He had had Roentgen examination by one or two inexperienced men, who were also practising internal medicine. The case was not recognized as cancer until a tumor developed. A careful roentgen examination should have shown the condition earlier and at a time more favorable for operation.

Case IV (123461).—Woman, aged fifty-one years. For five years before coming for examination this patient had had intermittent attacks of epigastric pain two hours p. c., lasting weeks or months, with intermissions of two to six months. For five months she has been vomiting whenever she ate a little more than usual, and during the past two months she has had epigastric pain immediately p. c. and at other times. Loss of weight 28 pounds in five months. Small, movable, tender mass in epigastrium. Hemoglobin, 85. Total acids, 20, all combined. *Roentgen findings:* Extensive filling defect involving both curvatures, extending well up into cardia, corresponding to palpable mass. No six-hour retention. Gaping pylorus (Fig. 4). *Diagnosis*: Inoperable cancer. No operation.

If this patient had been examined by Roentgen rays only a few months earlier there is little doubt that a diagnosis could have been made when surgery could offer some hope of cure.

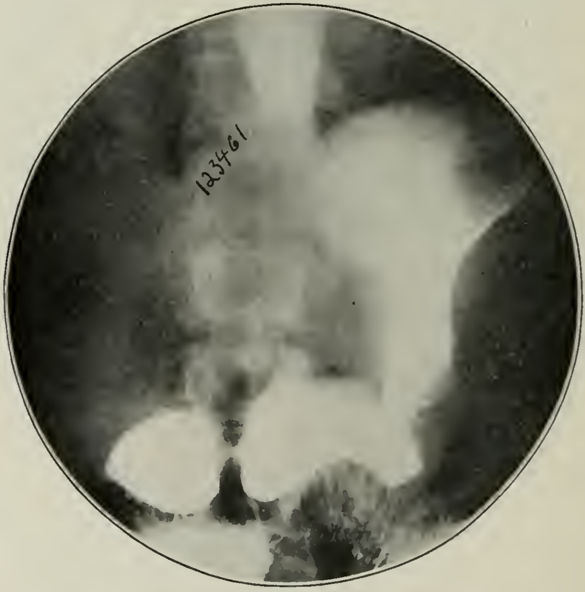

Fig. 4

Case V (86914).—Man, aged sixty-one years. From the age of eighteen to forty-two he had attacks lasting three to five weeks once a year of epigastric pain an hour or two p. c., with sour regurgitation, etc. One month ago he had an attack of pain with vomiting followed by fermentation and distress. Five days later at his home exploratory operation showed tumor of the stomach which was not removed. Loss of weight, 26 pounds. Total acids 54; free HCl, 4; combined, 50. Large, movable ridge in epigastrium. *Roentgen findings:* Stomach small, with marked filling defect in the pars media and pars pylorica, corresponding to a palpable mass. Retention of half the six-hour meal. Stomach somewhat fixed (Fig. 5). *Diagnosis:* Cancer. *Exploration:* Cancer of the pyloric end of the stomach; inoperable. *Pathologist's report:* Tissue removed, cancer.

This case shows how impossible it is to accomplish anything by surgery when such an advanced stage of the disease has been reached. The Roentgen rays were not at all necessary for a diagnosis in this case, but it showed the extent of involvement and its inoperability. Only by competent routine Roentgen examination of every person beyond cancer age with gastric symptoms, no matter how trivial, can the number of cases like the above be diminished.

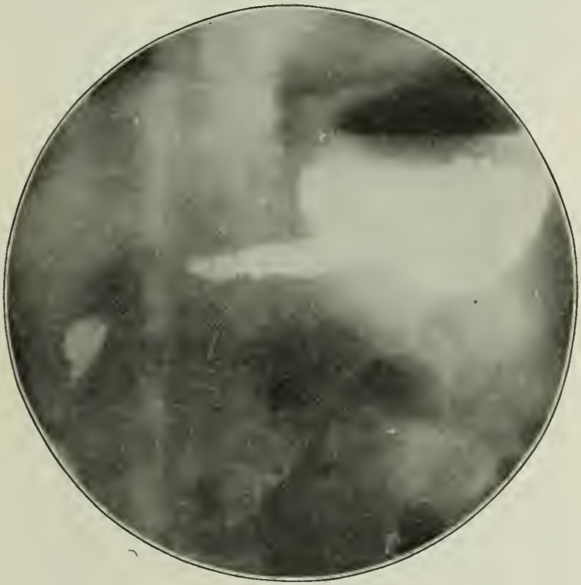

FIG. 5

CASE VI (117798).—Woman, aged sixty-six years. In the past five years this patient has had many attacks of grinding pain in the right abdomen, coming suddenly and lasting from a few to twelve hours. For four months she has had daily distress and sour vomiting soon after meals. Loss of weight, 30 pounds. Hemoglobin, 85. Total acids, 24; free HCl, 16; combined, 8. *Roentgen findings:* Prepyloric narrowing. Retention of half the six-hour meal. Active peristalsis. Some irregularity and thinning of barium shadow along the greater curvature in the pars media, due to gas in the colon (Fig. 6). The case was regarded as suspicious for a prepyloric lesion. A reray after belladonna was requested, and this examination showed a stomach normal in contour and without retention. *Operation:* Cholecystectomy; appendectomy. Cholecystitis with multiple papillomas; chronic appendix. *Pathologist's* *report:* Chronic cholecystitis with multiple papillomas. Chronic appendicitis.

This case illustrates the necessity of caution on the part of the radiographer. The prepyloric deformity and six-hour retention were due to gastrospasm as a reflex from the disease of the gallbladder. This sort of gastrospasm is of quite common occurrence, and extreme care is necessary in differentiating it from an actual lesion of the stomach. The active peristalsis in this instance rather suggested spasm and negated cancer.

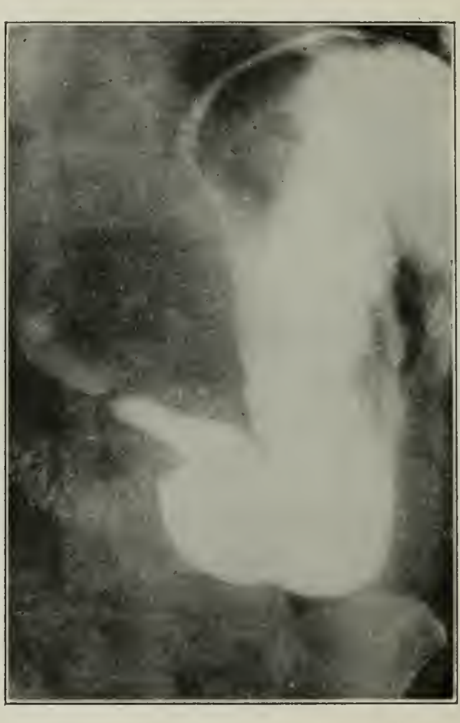

Fig. 6

Case VII (102013).—Woman, aged sixty-nine years. Two years ago this patient began to have discomfort after meals. A year later she noticed a lump in the epigastrium which has increased steadily in size. During the past eight months occasionally she has been nauseated and vomited when hungry. Loss of weight, 45 pounds. Hemoglobin, 85. Total acids, 6, all combined. Oblong mass in epigastrium. *Roentgen findings:* Small stomach without visible peristalsis. No retention. Lessened flexibility. Slight fixation. Lumen narrowed without marked irregularity of contour (Fig. 7). *Diagnosis:* Cancer. *Exploration:* Inoperable tumor involving the entire stomach (leather-bottle stomach). Some glandular thickening but no metastasis.

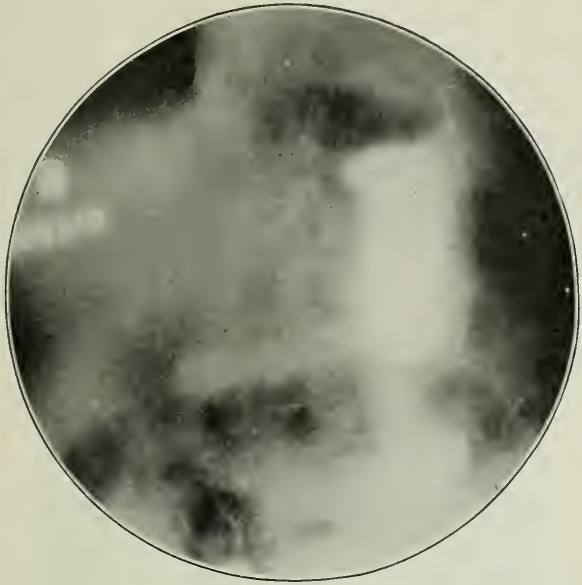

FIG. 7

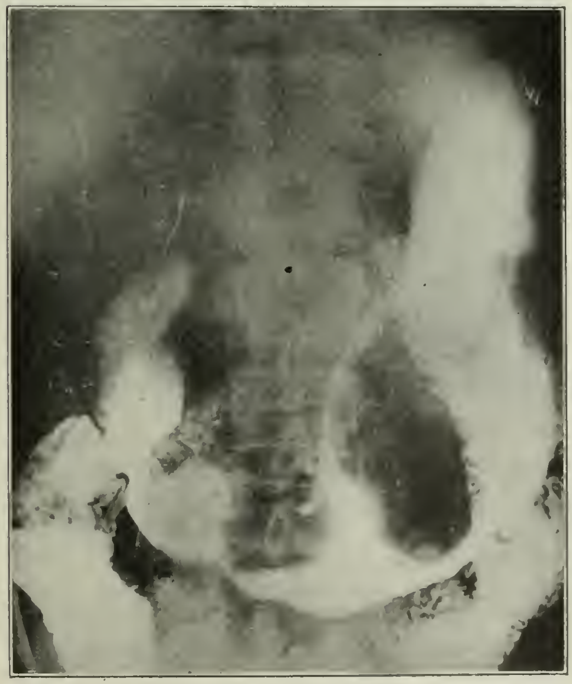

FIG. 8

Case VIII (124629).—Man, aged forty-four years. Eight months ago he began to have epigastric pain, coming a half-hour to one hour after meals. The pain continued until about six weeks ago; since then he has felt well, but worries over loss in weight (15 pounds). A firm tumor could be palpated to the left of the umbilicus, indefinite in outline, moving with respiration, and visibly modified in shape, evidently by peristalsis. Total acids, 66; free HCl, 60; combined, 6. *Roentgen findings:* Extensive filling defects in the pars media and pars pylorica. No retention from the six-hour meal (Fig. 8). *Operation:* Resection of three-fourths of the stomach (Mikulicz-Hartmann-Polya). Cancer, two large masses projecting from the posterior wall. *Pathologist's report:* Cancer; no glandular involvement found.

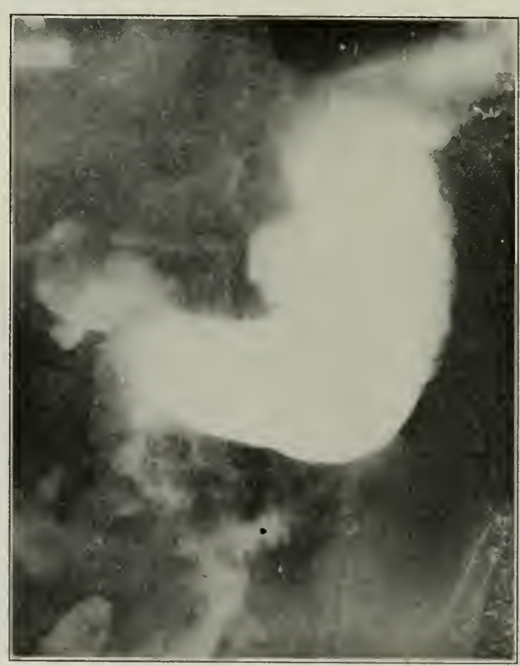

Fig. 9

Case IX (119622).—Woman, aged sixty years. For several years the patient has had, every five or six months, attacks of nausea and vomiting, without pain, lasting about a week. A similar attack began one month ago, at first without relation to food-taking, but during the past two weeks occurring a half to three hours after meals. No particular pain, but some epigastric soreness and burning. Loss of weight, 38 pounds in two years; mostly in the past two months. Hemoglobin, 76 per cent. Ridge in the left epigastrium palpable on deep inspiration. *Roentgen* *findings:* Very large niche on lesser curvature. Retention of half the six-hour meal (Fig. 9). *Diagnosis:* Cancerous ulcer. (The opinion as to malignancy was based upon the unusually large size of the niche.) No operation.

Case X (106071).—Woman, aged fifty-five years. For twenty years she has had attacks of severe epigastric, cramp-like pain, coming as often as every two weeks, lasting one or two hours, and without relation to food. For six months attacks have been more frequent; recently twice a day. Morphin for relief has been given. Vomiting of dark greenish fluid. Small, tender mass R. C. M. Loss of weight, 25 pounds. Hemoglobin, 85. Total acids, 40; free HCl, 28; combined, 12. *Roentgen findings:* Two examinations were made. The first showed marked irregularity of the pyloric end, without retention. The second examination, after giving belladonna showed practically the same condition (Fig. 10). *Diagnosis:* "Prepyloric irregularity; possible lesion; may be reflex." *Operation:* Cholecystectomy. Empyema of gall-bladder with stones. *Pathologist's report:* Cholecystitis. Cholelithiasis.

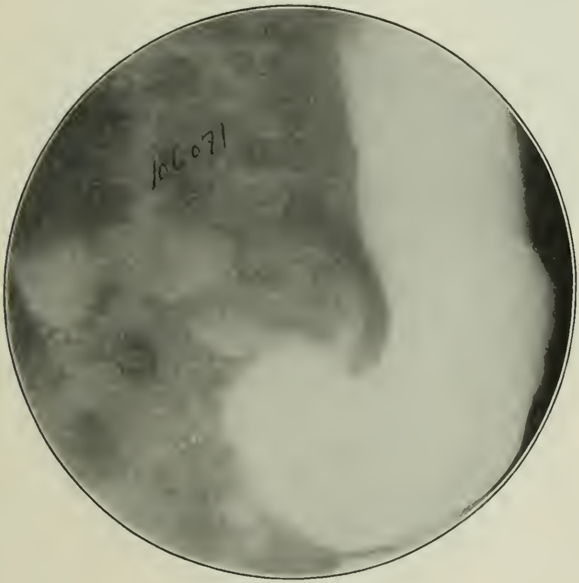

Fig. 10

The cautious diagnosis in this instance was due to the fact that the patient had an excellent history of gall-bladder trouble. The patient at the second examination showed no physiological effects from the belladonna, and it was felt that spasm could still not be wholly excluded. Further, an organic lesion of the stomach producing such prepyloric irregularity would probably also have resulted in a six-hour retention, antiperistalsis, palpable tumor, or other corroborative indication.

Case XI (106124).—Man, aged seventy years. Intermittent diarrhea for six months with 3 to 6 bowel movements daily. Occasional day or two of relief. Much sour belching. On rigid diet five months, with 40 pounds loss of weight. Occasional pain in the lower abdomen or stomach. Hemoglobin, 75. Total acids, 14, all combined. Stool report: No parasites. Proctoscopic negative. *Roentgen findings:* Filling defect in the pars pylorica. No six-hour retention (Fig. 11). *Diagnosis:* Cancer. *Operation:* Cholecystectomy. Large septic gall-bladder, with stones. Marked thickening of pyloric ring by spasm. *Pathologist's report:* Chronic catarrhal cholecystitis. Cholelithiasis.

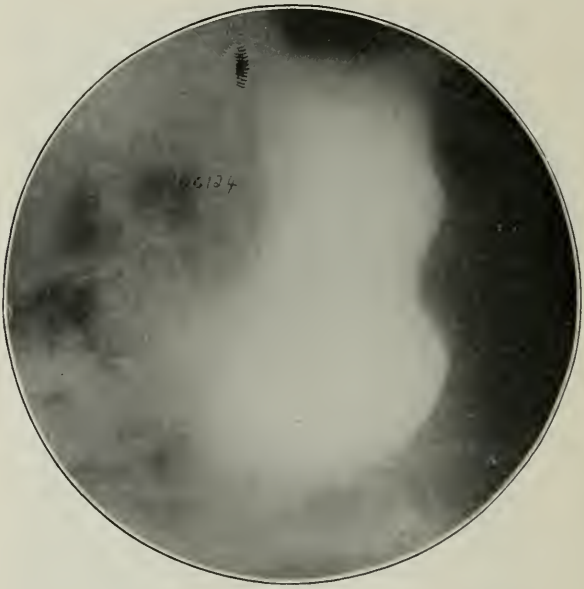

Fig. 11

Because of the patient's age and weakness the examination was effected with considerable difficulty. The findings, however, seemed quite definite and the possibility of spasm was not considered. The clinicians in charge of the case had considered it disease of the gall-bladder but upon the strength of the Roentgen-ray findings changed their diagnosis. The case is another illustration of the deceptiveness of gastrospasm.

Case XII (120996).—Man, aged fifty years. Two or three months ago he began to have intermittent attacks of dull epigastric pain one hour before meals, lasting three or four days, with remissions of four or five days. Food relief. Some pyrosis, pallor.

Slight edema of feet and legs for three or four weeks. No distinct loss of weight. Mass, right hypochrondrium. Total acids, 10; free HCl, 0; combined, 10; blood and mucus. Hemoglobin, 40 *Roentgen findings:* Plates made with the patient standing show small defect on the greater curvature in the pars media, while those made prone show two large central defects; with some irregularity and thinning of both curvatures. No retention from the six-hour meal (Fig. 12). *Diagnosis:* Cancer. *Operative findings:* Anterior gastro-enterostomy; stomach opened; base of tumors clamped. Four cancerous papillomas growing from the mucosa of the stomach, varying in size from that of a filbert to that of a lemon. *Pathologist's report:* Multiple papillomas; areas of cancer.

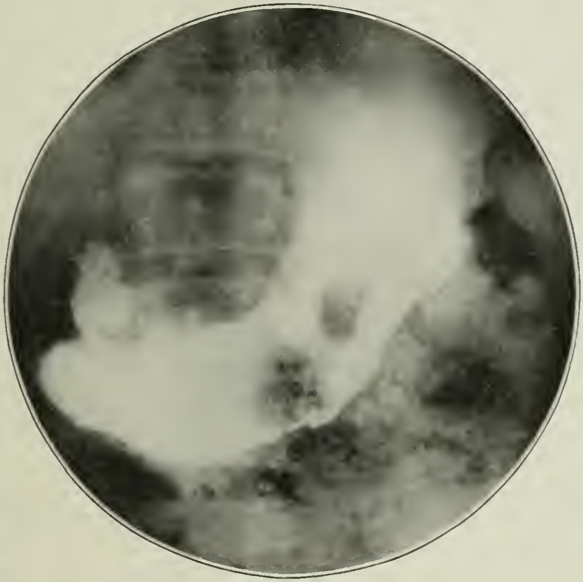

FIG. 12

THE SIGNIFICANCE OF ACRO-ATAXIA AND PROXIMO-ATAXIA.

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ACRO-ATAXIA is a term used to designate an impairment in the muscular sense of the intrinsic muscles of the hands and feet in contradistinction from ataxia of the proximal muscles of the upper and lower extremities.

The diagnostic significance of distinguishing between acro-ataxia and proximo-ataxia was first suggested in primary anemia when the differentiation brings out very striking symptoms. Patients with primary anemia complain of paresthesia in fingers and toes and impairment of fine manipulative movements long before there is any impairment in the grosser movements of the extremities. The lower extremities reveal this differentiation far more commonly than do the upper extremities. In the early period of primary anemia a patient will be unable to tell whether the great toe is being passively flexed or extended or twisted; but when the limb is elevated in various positions he will accurately indicate the position of the toe. The former test employs the muscular sense of the intrinsic muscles of the feet. The latter test employs the muscular sense of the iliofemoral muscles.

The anemic patient may lose all muscular sense in the intrinsic muscles of the feet and have no static ataxia, because the muscular sense of the iliofemoral muscles is unaffected. The anemic patient will have the muscular sense of the intrinsic muscles of the hand so impaired that buttoning a waist, washing dishes, sewing, and writing are laboriously and imperfectly accomplished; but when the finger-to-finger and finger-to-nose tests are tried, all indications of ataxia are wanting. In the latter instance we are testing the muscular sense of the thoracoscapular and scapulohumeral muscles to the exclusion of any function of the intrinsic muscles of the hands. Many patients with primary anemia with pronounced loss of muscular sense of intrinsic muscles of the feet and hands will voluntarily complain only of numbness and tingling, when direct questioning and testing will reveal a loss of the stereognostic sense which in a tabetic patient would render him incompetent for any occupation.

What first attracted my attention to the significance between acro-ataxia and proximo-ataxia was the surprising loss of the stereognostic sense in the hands and loss of all sense of position in the toes in anemic patients when there was not the slightest evidence of any loss of muscular sense in the proximal muscles of the upper or lower extremity, and for this reason the gait was not ataxic, there was no static ataxia, and with the exception of fine manipulations which employed only the hand muscles, there was no impairment of function in the upper extremities. In the later stages of anemia, proximo-ataxia and acro-ataxia are both present.

In spinal-cord disease we see just the reverse. Proximo-ataxia always precedes acro-ataxia. The tabetic patient will have a very pronounced loss of muscular sense in the iliofemoral muscles, with consequent symptoms, long before there is a loss of the sense of position in the toes. He will also lose the muscular sense in his thoracoscapular and scapulohumeral muscles before there is any loss of muscular sense in the hands. Acro-ataxia is seen only in advanced spinal-cord disease.

Primary anemia is a hemolytic disease in which the nervous system suffers, probably from the same toxic substance which acts as hemolysine. This suggests the possibility of employing the differentiation between acro-ataxia and proximo-ataxia as a diagnostic measure to distinguish peripheral nerve lesions from lesions in the spinal cord.

For the past four years all cases of primary anemia with neurological signs and all forms of neuritis, *e. g.*, alcohol, lead, diabetes, and diphtheria, and all syphilitic disease of the spinal cord have been carefully studied with this idea in view. The results have shown that acro-ataxia without proximo-ataxia is seen only in the primary anemias and peripheral neuritis. Proximo-ataxia without acro-ataxia is seen only in cord disease. In advanced stages of peripheral nerve and cord diseases both proximo-ataxia and acro-ataxia may be present.

This differentiation has served to recognize cases of alcoholic neuritis which have simulated spinal-cord disease. Acro-ataxia may also suggest primary anemia when the patient's color will not suggest anemia. In our cases there were also three diabetic patients with neuritic pains who would have been treated as diabetic neuritis had they not had proximo-ataxia which betrayed the spinal cord as the real seat of the disease. They proved to be cases of syphilis of the central nervous system with glycosuria as a symptom.

One case of carcinoma of the prostate afforded an interesting example of the value of this sign. The patient had mild diabetes for twelve years. An enlarged prostate caused residual urine for two years. During the past year the patient has had much pain in the distribution of both sciatic nerves in the thighs and legs. Proximo-ataxia without acro-ataxia indicated that the neurological signs were not of diabetic origin. The subarachnoid fluid proved to be normal, therefore the cord lesion was due to metastases from a carcinomatous prostate. The prostate was removed surgically and proved to be carcinoma on histological examination. The patient has made a good recovery from his operation, so the character of the spinal-cord lesion still remains in doubt, although at the operation a chain of enlarged lymph glands were palpated along the iliac vessels, a fact which lends additional probability to the carcinomatous character of the spinal-cord disease.

That toxic neuritis may cause proximo-ataxia without acro-ataxia is possible, but we have not had cases which have clearly shown such a combination of symptoms. But during the past four years, during which the relations between acro-ataxia and proximo-ataxia and cord and peripheral nerve disease have been observed, we have failed to find a single case of spinal-cord disease in which acro-ataxia existed unaccompanied by proximo-ataxia. When proximo-ataxia is unaccompanied by acro-ataxia, we have strong evidence that we are not dealing with a disease of the peripheral nerves.

During the past four years, at Lakeside Hospital we have had fifty-two cases of primary anemia, and in all of them in which neurological signs were presents there was either acro-ataxia alone or accompanied by proximo-ataxia. I have failed to find a single case of primary anemia in which proximo-ataxia existed unaccompanied with acro-ataxia. My experience with all cases seen outside the hospital has been the same.

Another striking experience occurred in primary anemia: Eighteen of the fifty-two cases at Lakeside Hospital were from fifty to sixty-seven years of age, and in sixteen of this number there are records of neurological signs. All these patients, with few exceptions, were seen by myself. In my private practice I have failed to find a single instance of primary anemia of fifty years or older which did not show some neurological signs. In patients under fifty years of age the anemia may be severe and last as long as four years without showing any neurological signs. The first neurological signs to appear in all the primary anemias are the loss of the vibratory sense in the distal portions of the upper or lower extremities and acro-ataxia.

Some of these patients never suffered from anemia. They were not pale, and their hemoglobin during the entire illness never went lower than 75 per cent., and this lasted only a few months. During most of the time there was from 80 per cent. to 95 per cent. hemoglobin (Talquist). The neurological signs, however, progressed just the same as in those patients who were very anemic. They were called primary anemia because they had a venous hum over the bulbus venosus, a high color index, leukopenia, and acro-ataxia and loss of perception of vibrations over the distal portions of the upper or lower extremities. In patients fifty years and older the primary anemia was frequently suggested by the neurological findings. Had it not been for acro-ataxia and impaired perception of vibrations the hematological phase of the disease would have been entirely overlooked.

The fact that the progress of neurological symptoms in primary anemia conforms to those developing in toxic neuritis suggests that the nervous affection in primary anemia begins in the peripheral nerves and ultimately involves the cord. Thus far there have been no histological examinations made which will confirm or deny this interpretation of clinical signs of the disease.

STUDIES OF NEPHRITIS.[1]

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During the past year and a half in the medical clinic of the Peter Bent Brigham Hospital we have been studying cases of chronic nephritis from several angles. Some of these studies have been published, others are ready for publication, while still others are incomplete. All these studies are more or less closely related to each other and form part of a somewhat systematic investigation of nephritis. Different members of the staff have taken up the study of special phases of the subject, and from time to time each has published the study which he has made. What we will present here represents part of our recent work. The several names that appear under the title are those of the men responsible for the work which is outlined here. In more detailed form each man will publish subsequently under his own name his own work.

A. Test Renal Meals in Relation to Renal Function. The ability of the kidney to excrete certain factors in the average normal diet has been utilized by many as a means of measuring renal function. The excretion of water, sodium chloride, and nitrogen has been tested by most observers. One method suggested by v. Monakow[2] has been to place the patient upon some form of diet which contains daily approximately the same amounts of sodium chloride, nitrogen, and water with a caloric value varying but little from day to day. In relation to this diet the twenty-four-hour amount of urine and its sodium chloride and nitrogen content have been quantitated. Then on different days these patients have received, in addition to the diet, 20 gm. of urea or 10 gm. of sodium chloride, and the ability of the kidney to excrete these added amounts of nitrogen and sodium chloride has been determined.

As in this test it is necessary for the patient to reach a certain degree of equilibrium of excretion after the diet has been begun before the added salt and nitrogen can be given, and as it is necessary to observe the excretion of these substances for at least two days after each is given, and as it is usual to allow the effect of the added amount of the one to end before adding the other, to carry out this test satisfactorily requires about ten days of accurate dieting with the patient in the hospital.

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[1] Presented at a meeting of the Association of American Physicians, held in Washington, D. C., May 11–13, 1915.

[2] Deutsch. Arch. f. klin. Med., 1911, cii, 248.

In 1914 Hedinger and Schlayer[3] published a paper in which the effect of diet on the excretion of water and sodium chloride was studied by submitting the patient for one day to a diet in which different meals contained varying amounts of water, sodium chloride, and nitrogen.[4] The urine was collected in two-hour periods through the day, and the water and sodium chloride were quantitated in each two-hour amount. The test renal meal day was preceded by two days on which the patient was on a light mixed diet containing from 8 to 12 gm. of NaCl, and with a fixed quantity of fluid, and on these days merely the excretion of water in relation to fluid intake was measured.

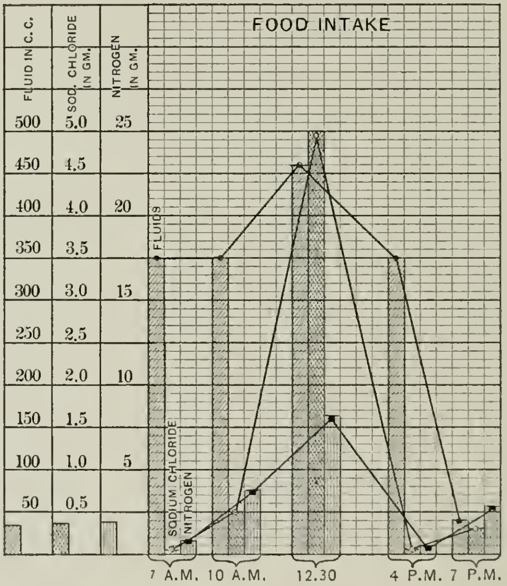

Chart I.—To show amounts of fluid, sodium chloride, and nitrogen in each meal of the renal diet. The lines connecting the tops of the columns give the curve of variation in intake of each constituent.

This form of test renal meals requires three days of the patient's stay in the hospital, but only on one day is accurate dieting necessary. The question naturally arises. Can as much information be obtained from the one test as from the other? If so, the shorter period of time required for the test of Hedinger and Schlayer would have a manifest advantage. During the past year we have investigated this question. We have modified the test as proposed by Hedinger and Schlayer by quantitating the nitrogen in the various portions as well as the water and sodium chloride, and we have changed slightly the composition of the meals on both the test day (Chart I) and on the two preceding days.[5]

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[3] Deutsch. Arch. f. klin. Med., 1914, cxiv, 120.

[4] In these meals the content of each also varied in food substances having a diuretic effect (water, salt, purins, etc.)

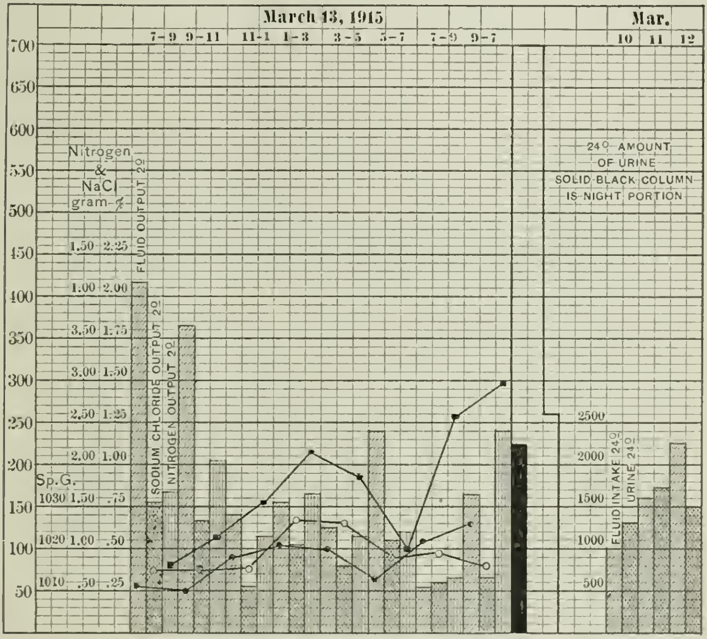

Chart II, Case I.—The series of columns beginning at the left give the amount of urine, sodium chloride, and nitrogen in each two-hour portion from 7 A.M. to 9 P.M., and in the portion from 9 P.M. to 7 A.M. The solid lines joining dots in the space of each column give the specific gravity of the urine and the percentage concentration of sodium chloride and nitrogen. Next is indicated the night portion of urine in relation to the total twenty-four-hour amount. The columns at the right give the fluid intake and urine output in the days preceding the test day.

Without entering at this time into any discussion as to the value of such test renal meals in determining the renal function, we will discuss comparatively the results obtained in the two forms of tests carried out on the same patient. On sixteen patients with chronic nephritis both tests were carried out in a complete form. In addition to these patients a variety of other methods of testing renal function were applied. In an equal number of cases only the Hedinger and Schlayer test renal meal method was applied in connection with other forms of renal functional tests. The results of all of these tests from the point of view of estimating the function of the kidney and the relative value of each will be discussed by Dr. O'Hare when he publishes a detailed statement of this work.

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[5] On the test day we have used the following menu for the several meals:

7 A.M. Coffee, milk, sugar, toast, and butter.

10 A.M. Milk, toast and butter.

12.30 P.M. Bouillon, broiled steak, butter, mashed potato, butter, toast and butter, coffee, milk and sugar.

4 P.M. Tea, milk, sugar, crackers.

7 P.M. Soft egg, blanc mange (one egg, sugar, corn starch, milk) cream, in amount to give approximately total calories 2500, total fluids, 1550 c.c., total protein 76 gm., total fats 127 gm., total carbohydrates, 245 gm., total sodium chloride, 5.8 gm. On the two days preceding the test day the patient usually has a diet containing 2000 calories, 75 gm. of protein, and 4 gm. of sodium chloride.

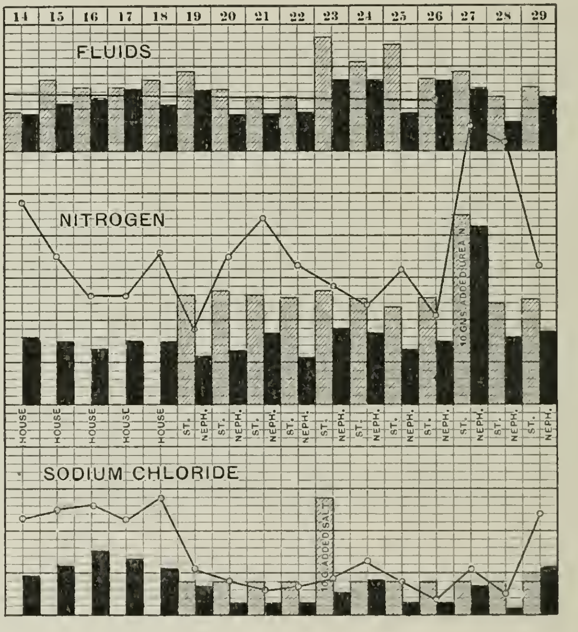

Chart III, Case I.—The hatched columns indicate intake; the solid columns output. The upper series are for fluids, the middle for nitrogen, and the lower for sodium chloride. The added salt and added urea are indicated by the lengthening of the columns of intake.[6]

We have found that these two forms of testing renal function in relation to test diets agree quite well in their results. (Case I, Chart II and III; Case II, Chart IV, and V; Case III, Chart VI and VII; Case IV, Chart VIII and IX). That the results very closely agree in any quantitative sense is, of course, not to be expected, for we have found that if we gave added salt or added urea on several occasions to our patients on a standard diet the results obtained are rarely quantitatively identical, but there is generally a striking similarity in the results from period to period. (Charts VII and XII.)

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[6] "House" indicates a general mixed diet; "St. neph." indicates a diet of about 2000 calories, containing 75 gm. of protein and 4 gm. of sodium chloride.

In the same way we have repeated the Hedinger and Schlayer test renal meal on the same patient and found very considerable variations in the curve of excretion of the various components which were quantitated (Case V, Charts X and XI), but at the same time there is enough similarity in the different periods to justify the same conclusions as regards the ability of the kidney to excrete the various components when no extraneous factors in the interval between the tests had come in to alter the character of the result.

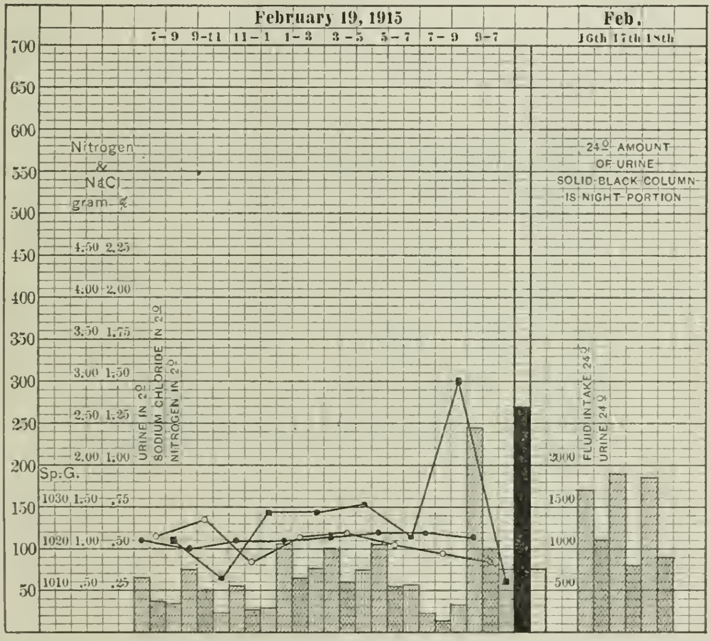

CHART IV, Case II.—The series of columns beginning at the left give the amount of urine, sodium chloride, and nitrogen in each two-hour portion from 7 A.M. to 9 P.M., and in the portion from 9 P.M. to 7 A.M. The solid lines joining dots in the space of each column give the specific gravity of the urine and the percentage concentration of sodium chloride and nitrogen. Next is indicated the night portion of urine in relation to the total twenty-four-hour amount. The columns at the right give the fluid intake and urine output in the days preceding the test day.

Perhaps there has been a somewhat closer agreement between the two tests in regard to the salt excretion than has been found in the nitrogen excretion. It has been our experience that the ability of the kidney to excrete salt is decreased much earlier than is the case with nitrogen, and many more of our cases have shown an inability to excrete salt well than has been the case with the nitrogen. This may possibly explain the greater variation in the results with the nitrogen in these cases which we have studied.

The cases with advanced nephritis, as judged by other tests and the general condition of the patient, by the Hedinger and Schlayer test diet show strikingly a tendency to fixation in the concentration of the urine as measured by the specific gravity, with a relatively slight variation in the amount passed in each two-hour period. In some cases this fixation in specific gravity has occurred at a low level (Chart VIII) and in others at a fairly high level (Chart IV). In the same way some patients have shown but slight variation in amount of their urine from period to period with either a very small amount or a fairly large amount in each period. Fixation of salt concentration has occurred in the more severe cases and usually at a low level of excretion. In the longer test, with added salt and added urea, the fixation of specific gravity and the lack of variation in the quantity of the urine is not so apparent.

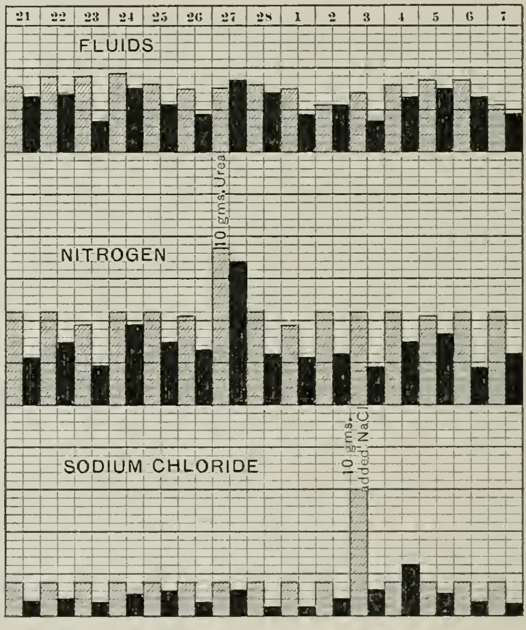

CHART V, Case II.—The hatched columns indicate intake; the solid columns output. The upper series are for fluids, the middle for nitrogen, and the lower for sodium chloride. The added salt and added urea are indicated by the lengthening of the columns of intake.

The inability of the kidney to satisfactorily excrete salt is shown in both tests (Charts VI, VII, VIII, and IX). The same things are true with regard to the nitrogen (Charts VI, VII, VIII, and IX), though there has been less tendency to either fixation in the concentration of the nitrogen or constancy in the amount of nitrogen in each two-hour period.

Both forms of dietary renal tests are of limited application in the sense that cases of severe nephritis often are unable to take the diet on account of lack of appetite or developing nausea. In each form of test the amount of laboratory work is approximately the same. The only distinct advantage of the one over the other is in the shorter period required for the Hedinger and Schlayer test. It is to be remembered that not exactly the same form of test is being applied, because in the one the chief factor in the test consists in seeing what the ability of the kidney is to excrete a single substance added to a diet containing only a moderate amount of that given substance along with other constituents. In the other test the excretion of several substances contained in a varying admixture of food constituents is being studied over a much shorter period of time. It might be that the results from the two kinds of tests would be more nearly comparable if in the longer test both added nitrogen and

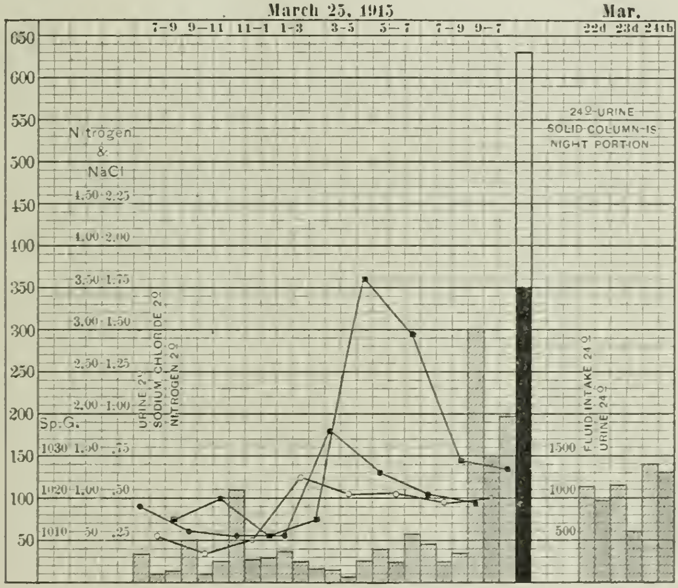

Chart VI, Case III.—The series of columns beginning at the left give the amount of urine, sodium chloride, and nitrogen in each two-hour portion from 7 A.M. to 9 P.M. and in the portion from 9 P.M. to 7 A.M. The solid lines joining dots in the space of each column give the specific gravity of the urine and the percentage concentration of sodium chloride and nitrogen. Next is indicated the night portion of urine in relation to the total twenty-four-hour amount. The columns at the right give the fluid intake and urine output in the days preceding the test day.

added sodium chloride were introduced into the diet on the same day.

In the Hedinger and Schlayer test the results in a case of nephritis cannot be compared in any quantitative sense with what might be termed a normal curve of excretion. Normality consists with this diet in the ability to vary from period to period the amount of water, its specific gravity, the amounts of salt and nitrogen and their percentage concentration rather than to show any definite type of curve of excretion of each. Abnormality consists in a more or less degree of fixation in all of these values or in certain ones of them.

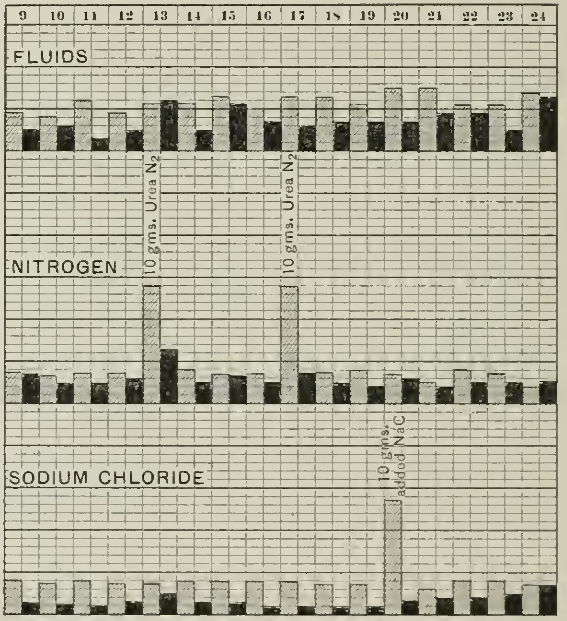

Chart VII, Case III.—The hatched columns indicate intake, the solid columns output. The upper series are for fluids, the middle for nitrogen, and the lower for sodium chloride. The added salt and added urea are indicated by the lengthening of the columns of intake.

Our general feeling has been that a study of the salt and nitrogen excretion by means of test diets is relatively of less use in determining the prognosis than are some of the other functional tests, such as the phenolsulphonephthalein excretion and the amount of blood nitrogen. This is not because the severe cases fail to show quite definite changes in their excretion, but because the other tests give fully as much information at a much less cost of labor and time. In the milder cases where phenolsulphonephthalein excretion is fair and blood nitrogen low in amount, disturbances in excretion of water, salt, or nitrogen are found; the correct interpretation of this cannot be given until time enough has elapsed to show how these cases progress.

With regard to anatomical diagnosis, we think that a study of salt nitrogen, and water excretion will give very little aid. They serve to subdivide cases of chronic nephritis in a functional sense; the value of so subdividing the cases remains to be shown.

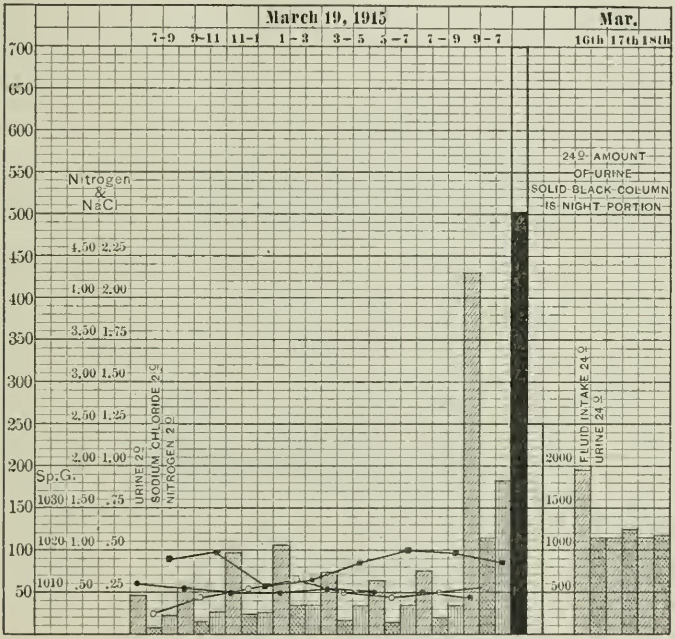

Chart VIII, Case IV.—The series of columns beginning at the left give the amount of urine, sodium chloride, and nitrogen in each two-hour portion from 7 A.M. to 9 P.M., and in the portion from 9 P.M. to 7 A.M. The solid lines joining dots in the space of each column give the specific gravity of the urine and the percentage concentration of sodium chloride and nitrogen. Next is indicated the night portion of urine in relation to the total twenty-four-hour amount. The columns at the right give the fluid intake and urine output in the days preceding the test day.

B. Quantitative Studies of Non-protein Nitrogenous Bodies of the Blood. In a series of eighteen patients (Charts XIII, XIV, and XV) with nephritis the total non-protein nitrogen of the blood was determined and also the ammonia nitrogen, urea nitrogen, uric acid nitrogen, creatinin, and combined creatinin and creatin nitrogen, and in most of the cases the amino-acid nitrogen. It was found in this series that the urea nitrogen increased usually in proportion as the total non-protein nitrogen increased and averaged 63.4 per cent. of the total. Ammonia nitrogen increased slightly as the total non-protein nitrogen rose, but this rise was not proportional. Creatinin showed roughly a proportionate increase while amino-acid nitrogen showed no constant increase. Uric-acid nitrogen increased only very slowly, with an increase in total non-protein nitrogen, and the increase was not regular or proportionate to that of the total non-protein nitrogen. In those cases (14) in which amino-acids were quantitated the sum total of urea, ammonia, uric acid, creatinin, creatin, and amino-acid nitrogen was subtracted from the total non-protein nitrogen to give a figure for residual or unknown nitrogen. It has been pointed out by others that such a nitrogen portion might contain the toxic element in nephritis, and so should be largest in those cases with most evident toxemia. In our figures it was roughly proportionate to the clinical severity of the case. However, it is quite evident that summation of errors in individual determinations may be responsible in part for the amount of residual nitrogen. Furthermore, if there is a marked retention of non-protein substances it is probable that other substances known to be non-toxic not quantitated in our work may have caused all this increase, and the figure means only what a rise in total non-protein nitrogen means.

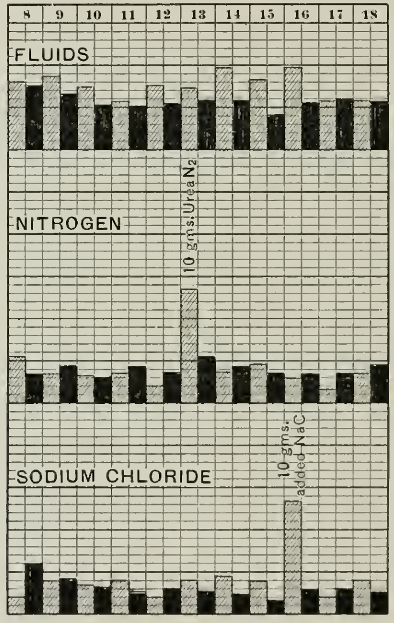

CHART IX, Case IV.—The hatched columns indicate intake, the solid columns output. The upper series are for fluids, the middle for nitrogen, and the lower for sodium chloride. The added salt and added urea are indicated by the lengthening of the columns of intake.

In these same cases the total non-protein nitrogen and the urea nitrogen of the spinal fluid were determined. With the exception of two cases with anuria (Cases VIII and IX, Chart XII) the total non-protein nitrogen of the spinal fluid averaged about 25 per cent. lower than that in the blood, while the urea nitrogen in each had almost identical values. It would seem from this that urea is the only one of the nitrogenous bodies readily excreted into the spinal fluid, and that quantitation of spinal fluid nitrogen adds but little information to that obtained from quantitations of blood nitrogen. In all of these patients the condition of the retina was carefully studied. It was found that albuminuric retinitis occurred at any level of nitrogen retention, and there was no relation between its occurrence and the proportionate amount of any of the nitrogen bodies quantitated. Certainly, there was found no evidence of a

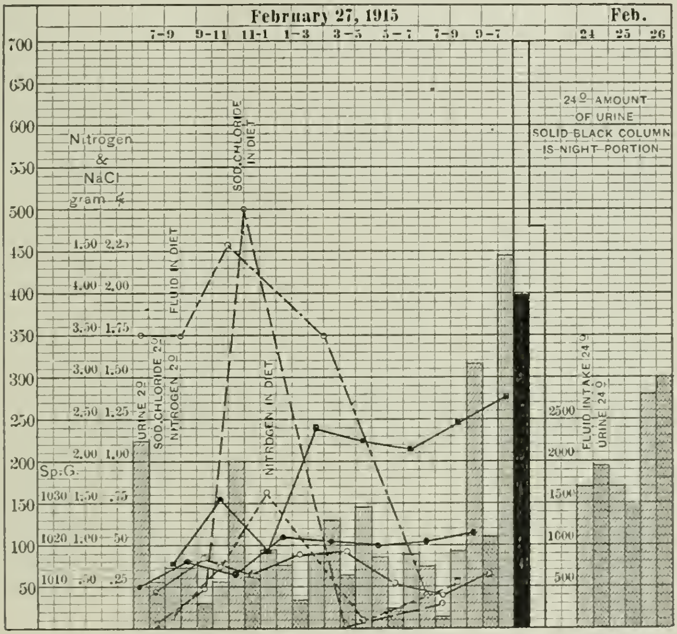

Chart X, Case V.—The series of columns beginning at the left give the amount of urine, sodium chloride, and nitrogen in each two-hour portion from 7 A.M. to 9 P.M., and in the portion from 9 P.M. to 7 A.M. The solid lines joining dots in the space of each column give the specific gravity of the urine and the percentage concentration of sodium chloride and nitrogen. Next is indicated the night portion of urine in relation to the total twenty-four-hour amount. The columns at the right give the fluid intake and urine output in the days preceding the test day. The broken lines joining dots indicate the amounts of fluid, sodium chloride, and nitrogen in each meal. In the case of nitrogen in the meals the scale is not the same as that of the nitrogen in the portions of urine, but is greater, corresponding to the scale in Chart I.

causal relation between any of these nitrogenous bodies and albuminuric retinitis.

C. Diuresis in Relation to Diuretics. From our clinic have been published several papers on the effect of diuretic drugs on animals with experimental nephritis.[7] All together these have shown that the ordinary diuretics are either ineffectual or harmful to animals with these acute renal lesions. The results of these experiments have made us skeptical as to the benefit of diuretic drugs in human nephritis, and so we have been examining our records of patients to see if this skepticism was justified or not.

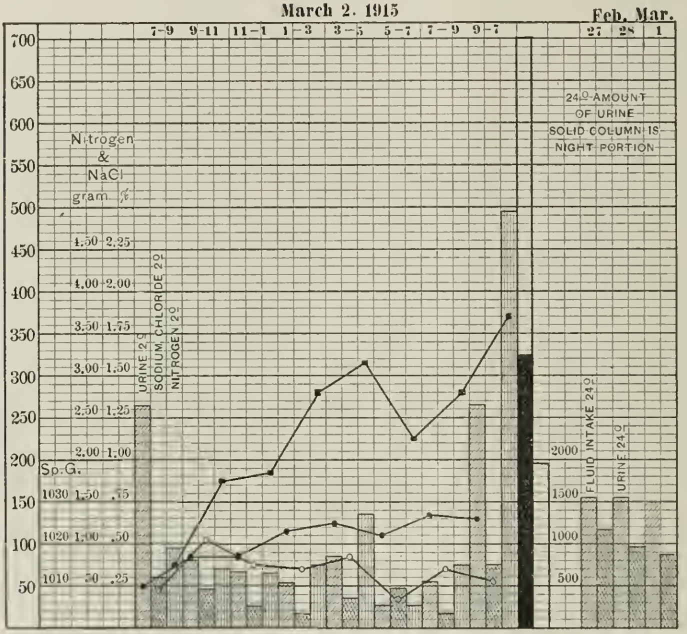

Chart XI, Case V.—The series of columns beginning at the left give the amount of urine, sodium chloride, and nitrogen in each two-hour portion from 7 a.m. to 9 p.m., and in the portion from 9 p.m. to 7 a.m. The solid lines joining dots in the space of each column give the specific gravity of the urine and the percentage concentration of sodium chloride and nitrogen. Next is indicated the night portion of urine in relation to the total twenty-four-hour amount. The columns at the right give the fluid intake and urine output in the days preceding the test day.

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[7] Christian, Diuretic Drugs in Acute Experimental Nephritis, Jour. Amer. Med. Assoc., 1913, lxi, 267. Chrisitian and O'Hare, A Study of the Therapeutic Value of a Diuretic (Theobromin Sodium Salicylate) in Acute Experimental Nephritis, Arch. of Int. Med., 1913, xi, 517. Walker and Dawson, The Effect of Diuretic Drugs on the Life of Animals with Severe Acute Nephritis, Arch. Int. Med., 1913, xii, 171. Christian, The Effect of Theobromin Sodium Salicylate in Acute Experimental Nephritis as Measured by the Excretion of Phenolsulphonephthalein, Arch. Int. Med., 1914, xiv, 829. Fitz, The Immediate Effect of Repeated Doses of Theobromin Sodium Salicylate and Theocin on Renal Function in Acute Experimental Nephritis, Arch. Int. Med., 1914, xiii, 945.

For some time it has been the routine custom on the medical service of the Peter Bent Brighan Hospital to measure and chart both the fluid intake and urine output of all patients. From these observations an idea may be obtained of diuresis in the average types of cases such as are admitted to a general hospital. Any patient in whom the urine output in twenty-four hours was 1600 c.c or over is regarded as having a diuresis; furthermore, any patient in whom the urine output in twenty-four hours exceeds the fluid intake is considered to have a diuresis. Diuresis in this sense occurred on at least one day in about 15 per cent. of 600 successive patients. Of the 89 patients among these 600 who showed diuresis, the largest group, 32, were cases of chronic cardiac disease, with decompensation in which, with digitalis, limitation of fluid intake and rest, diuresis followed. Next in order came cases of chronic nephritis, 22 in number. Diuresis in this group will be discussed more in detail later. Six patients had diabetes and seven typhoid; in both, diuresis was due to increased fluid intake. The others were miscellaneous cases in which it was often difficult to even surmise as to the direct cause of the diuresis. In this group are patients with diuresis during convalescence from pneumonia and from

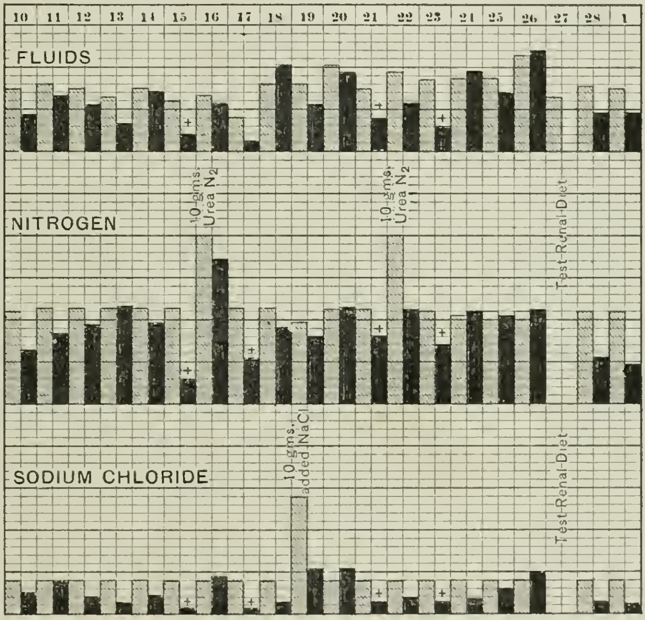

CHART XII, Case V.—The hatched columns indicate intake, the solid columns output. The upper series are for fluids, the middle for nitrogen, and the lower for sodium chloride. The added salt and added urea are indicated by the lengthening of the columns of intake.

CHART XIII.—TABLES SHOWING DETERMINATIONS OF NITROGENOUS BODIES IN BLOOD AND SPINAL FLUID IN CASES OF CHRONIC NEPHRITIS WITH NORMAL EYE-GROUNDS.

No.	Hosp. Med. No.	Blood.									Spinal fluid.		Blood pressure.	Phthalein excretion in 2 hours.	Remarks.
		Total non-protein nitrogen	Urea nitrogen.	Ammonia nitrogen.	Uric acid nitrogen.	Creatinine nitrogen.	Creatine nitrogen.	Amino acid nitrogen.	Residual nitrogen.	Chlorides in gms.	Total non-protein nitrogen.	Urea nitrogen.			
1	2358	26.77	14.38	0.09	0.40	0.77	0.99	6.78	3.36	0.4476	17.85	11.09	130–85	48%	Normal control.
2	2319	29.43	15.63	0.15	0.34	0.57	0.65	5.42	6.67	0.4435	24.68	15.45	240–160	47%	
3	2357	35.70	18.49	0.10	0.67	0.67	0.95	8.44	6.38	0.4391	27.35	18.50	210–108	52%	Chronic myocarditis.
4	2348	43.48	23.57	0.12	0.40	0.59	1.19	6.52	11.09	0.4707	35.70	21.25	185–95	52%	
5	1992	55.30	38.98	0.14	0.67	3.07	4.27	.....	.....	0.5153	......	......	260–110	12%	
6	1954	57.60	36.85	0.15	0.64	0.82	5.70	.....	.....	0.4296	......	......	235–115	21%	
7A	2006	95.27	66.66	0.15	0.64	3.68	2.89	.....	.....	0.5363	......	......	190–98	Unreadable trace	
7B		90.90	62.50	0.19	0.53	5.08	2.32	6.42	13.86	0.5682	66.66	60.24	190–100	Unreadable trace	
8	2259	128.00	95.10	0.16	0.68	5.29	7.08	5.89	13.80	0.3429	128.00	95.21	130–80	.....	Mercury poisoning.
9	2174	138.10	79.76	0.24	1.67	4.09	4.37	16.32	31.65	0.4216	142.96	85.88	185–140	Unreadable trace[8]	

7A on December 12. 7B on December 17.

CHART XIV.—TABLES SHOWING DETERMINATIONS OF NITROGENOUS BODIES IN BLOOD AND SPINAL FLUID IN CASES OF CHRONIC NEPHRITIS HAVING ONLY VASCULAR CHANGES IN THE EYE-GROUNDS.

10	2132	47.51	29.58	0.18	0.40	2.02	3.58	10.23	1.52	0.4500	......	......	265–140	33%	
11	2202	71.43	43.07	0.11	0.66	1.71	2.10	6.50	17.28	0.5362	47.62	40.32	245–150	18%	17 cells in spinal fluid
12	2316	95.23	60.00	0.16	0.43	3.68	4.34	8.05	18.57	0.4649	80.00	60.16	213–124	Unreadable trace	

CHART XV.—TABLES SHOWING DETERMINATIONS OF NITROGENOUS BODIES IN BLOOD AND SPINAL FLUID IN CASES OF CHRONIC NEPHRITIS WITH MARKED ALBUMINURIC RETINITIS.

13	2354	23.81	14.60	0.10	0.35	0.61	0.99	4.02	3.14	0.4243	20.00	12.50	285–160	28%	Apoplexy.
14	2074	40.98	27.00	0.17	0.39	1.67	2.21	5.22	4.32	0.4400	33.28	26.32	180–130	19%	
15A	2043	54.05	32.14	0.12	0.46	2.74	2.74	.....	.....	0.4558	43.46	26.59	250–166	10%	
15B		60.61	41.54	0.12	1.26	2.30	3.12	10.64	1.63	0.4735	46.58	31.25	250–160	10%	
16A	2108	55.55	29.35	0.09	0.60	2.63	1.59	9.44	11.85	0.4407	37.21	27.77	190–150	15%	4 cells per cm. in spinal fluid.
16B		47.54	25.50	0.15	0.98	2.45	3.66	6.56	8.24	0.3997	33.33	26.00	150–130	11%	Herpes zoster complicating uremia. 91 cells per cm. in spinal fluid.
17A	1882	192.30	113.80	0.20	0.62	8.01	14.39	.....	.....	0.4788	125.00	111.11	248–128	Unreadable trace	16 cells per cm. in spinal fluid.
17B		266.66	166.45	0.21	2.78	7.85	7.66	.....	.....	0.5141	188.69	166.66	250–130	Unreadable trace	Uremia. 23 cells per cm. in spinal fluid.
18	1975	257.70	181.80	0.33	1.51	6.01	30.93	.....	.....	0.4752	......	......	208–152	Unreadable trace	Uremia.

15A on December 19. 15B on December 30. 16A on January 4. 16B on January 19. 17A on November 30. 17B on December 14.

[8] Phthalein estimation made three weeks previously at Massachusetts General Hospital.

attacks of bronchial asthma; patients with Hodgkin's disease, general carcinomatosis of the long bones, carcinoma of the head of the pancreas; pleurisy with effusion long after the pleural fluid had been removed mechanically; tabes in a patient requiring catheterization; meningitis; pernicious anemia following transfusion, migraine, etc.

In the records of successive patients as used above are included many records of individuals who were in the hospital for short periods of time in which only relatively few observations of fluid output were made; so our figures based on these 600 successive patients very likely give an incorrect idea of the frequency of diuresis, indicating that it is less common in the average hospital patient than is really the case. To avoid any error incident to very brief stay under observation, another series of successive records were gone over and all charts of patients who remained in the hospital not less than seven completed days were examined.

A series of 117 such were studied. Of these 69, or 59 per cent., on at least one day showed an output of urine in excess of 1600 c.c., or in excess of fluid intake; while 48, or 41 per cent., did not. In making this division the first day in the hospital is not included, as it often represents an incompleted twenty-four hours. Furthermore, the urinary excretion of the first day frequently is influenced by the excitement of admission to the hospital and by other extraneous factors. It is to be remembered in this connection that we have defined diuresis in a very limited way. In the figures just given numerous factors enter to make the number showing diuresis relatively large. For example, in twenty cases of this group on only one day did the urine exceed, and then but slightly, the fluid intake. This happened on days when for some reason or other the patient drank relatively little fluid, but the total urine on these days when it had exceeded the fluid intake was well below 1600 c.c. in amount. We think that these cases justly may be excluded from the group regarded as showing a diuresis. If this is done the number showing a diuresis represents 41 per cent. of the total. In a number of other cases urinary output was only once slightly above 1600 c.c., or in a long stay in the hospital only occasionally did the urine exceed the fluid intake. Going over the cases in this way there was a definite diuresis in relatively few of the cases, naturally slightly more than in the group in which were included cases in the hospital for only a short stay, but still proportionately a small number.

The analysis of the 600 successive cases given above indicated that chronic cardiac involvement, chronic nephritis, typhoid, and diabetes most often were the conditions in which diuresis occurred. The same conditions were found most commonly as the diagnosis in the patients of this second group showing diuresis. An examination of another group of 100 records in a way similar to the second series gave very similar figures.

The striking things in going over these cases have been the relative infrequency of diuresis even of only short duration in our hospital patients, and the lack aside from digitalis or large fluid intake of an easily assignable cause for such diuresis as occurred. It seemed that possibly a study of a group of cases of nephritis with relation to diuresis might throw some light on the question, inasmuch as this was the only group aside from cases of cardiac insufficiency in which diuresis occurred with any frequency. Consequently, 100 consecutive cases with chronic nephritis who had remained in the hospital not less than one week were examined.

Of these 100 cases of chronic nephritis, 51 showed no diuresis in the sense described above, while 49 had diuresis on at least 1 day. Almost all of the cases of chronic nephritis had hypertension, and 47 of them showed evidence of cardiac lesion diagnosed either as chronic myocarditis or chronic valvular lesion of some kind. This diagnosis of cardiac lesion was based on either definite evidence of cardiac decompensation or on electrocardiographic evidence of disturbance in myocardial function. Of the 100 cases of chronic nephritis, 43 received no diuretic therapy (increased fluid intake, digitalis, theocin, or similar drugs), and of these 12 showed a diuresis while 31 did not; 29 patients received digitalis; 17 with an ensuing diuresis, 12 without diuresis. Of the 17 cases in whom digitalis produced a diuresis, 14 showed very definite evidence of cardiac lesion, while in 2 cardiac decompensation was very probably present as they were cases with hypertension with signs of edema at the bases of the lungs as well as subcutaneous edema. In the one remaining case of this group there was a normal blood-pressure and no signs of cardiac lesion and no physical findings to suggest cardiac decompensation. In 8 patients a large fluid intake resulting from thirst caused diuresis. In three patients given sodium bicarbonate it appeared to cause diuresis. In 4 patients on a standard nephritic diet, diuresis occurred when either 10 grams of sodium chloride or 20 grams of urea were added to the diet. Particularly interesting are 10 cases in which such diuretic drugs as theobromin sodium salicylate, potassium citrate, caffein, and theocin produced no diuresis.

Curiously enough, in the 100 cases of chronic nephritis these so-called diuretic drugs failed very generally to produce diuresis when used alone. Occasionally when they had been used in conjunction with digitalis there was a diuresis, and here the digitalis alone may have been the cause of the diuresis. The number of cases is, of course, too small to justify the conclusion that this group do not act as diuretics in the condition of chronic nephritis, but these findings justify further our feeling of skepticism, and we hope that they will stimulate renewed study of the problem of the action of diuretics.

Most of the patients in this group had slight if any edema. Possibly this is the cause of so many failures to obtain diuresis in cases without cardiac failure. If so, then diuretic drugs would seem to have little value as eliminants of toxic substances in chronic nephritis without edema. Further evidence certainly is needed on this point to justify the use of diuretics in uremic conditions without edema in view of the evidence which has been accumulated that the diseased kidney is abnormally sensitive to fatigue and that diuretics may cause fatigue and consequent decrease in renal excretion, while in animals with acute lesions they are often demonstrably harmful. However, diuretic drugs do not have even any very constant effect in cases of nephritis with edema and without cardiac decompensation, as is shown by the following cases:

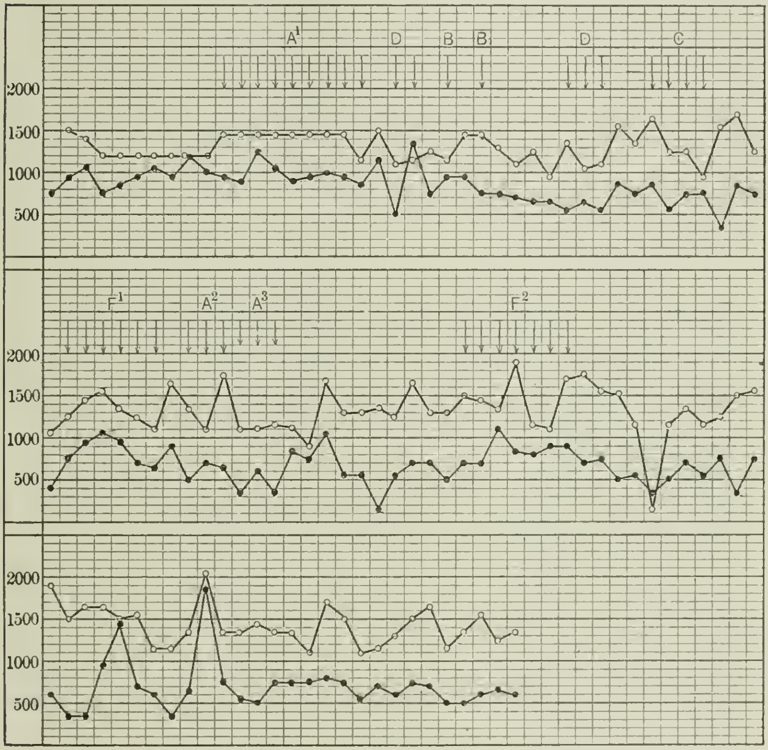

Chart XVI.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under A^1 indicates a day on which the patient received three doses of 0.1 gm. each of powdered digitalis leaves; under A^2 a day on which the patient received two doses of the same, and under A^3 a day on which the patient received two doses of 0.05 gm. each of powdered digitalis leaves. Each arrow under B indicates a dose of 0.5 gm. of theocin; under C a day on which the patient received 0.13 gm. of caffein citrate every four hours; under D a dose of 0.5 gm. of theobromin sodium salicylate; under F^1 a dose of 1 gm. of potassium citrate, and under F^2 a day on which the patient received two doses of 0.5 gm. each of potassium citrate.

A boy, aged nineteen years (Peter Bent Brigham Hospital, Medical No. 1225, Chart XVI and XVII), came into the hospital complaining that for about a week he had had edema of his legs, abdomen, back, and cheeks. When he came in his blood-pressure was 160 mm. of mercury. There was evidence of a moderate amount of fluid in his abdomen and in his thorax, and there was the edema of the subcutaneous tissue of which he complained. There was a slight degree of exudation in the retina of one eye. His urine contained a large amount of albumin, many cellular and granular casts, and a few red-blood cells. His phenolsulphonephthalein excretion in two hours was 34 per cent. His total non-protein nitrogen was 35 mgm. per 100 c.c. of blood. He came into the hospital on May 20 and remained until September 9. During this time his phenolsulphonephthalein excretion fluctuated between the figure given above and a minimum figure of 15 per cent. in two hours; whereas his blood nitrogen fluctuated between 35 mgm. and

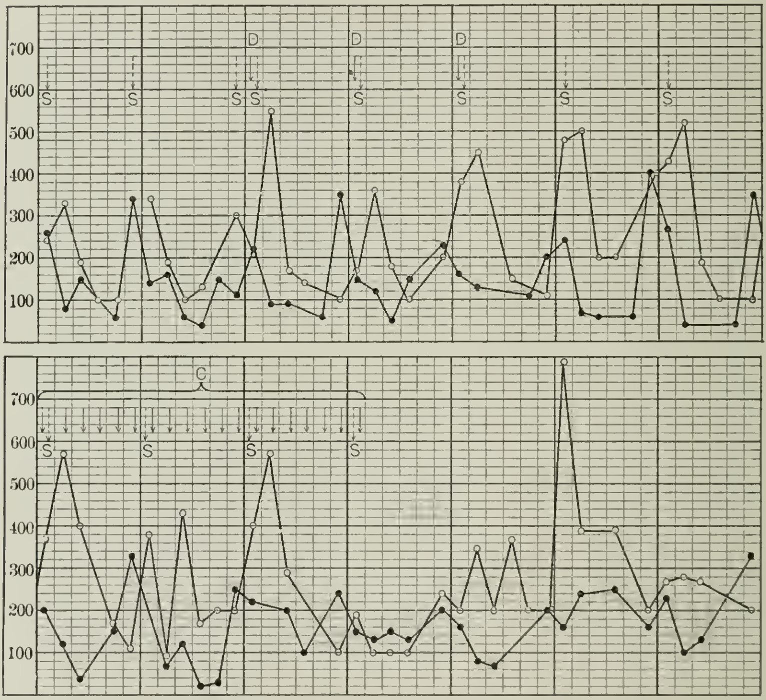

Chart XVII.—The solid black dots indicate the four-hour amount of urine in cubic centimeters. The black circles indicate the four-hour amount of fluid intake in cubic centimeters. Each arrow under C indicates one dose of 0.13 gm. of caffein citrate, and under D indicates a dose of 0.5 gm. of theobromin sodium salicylate. Each arrow over S indicates an electric light sweat bath in bed.

44 mgm. per 100 c.c. of blood, with one reading of 71 mgm. per 100 c.c. of blood at a time when there was no other evidence of increased renal insufficiency. During his stay in the hospital the amount of albumin in his urine gradually decreased in amount, and the edema in various parts of his body all disappeared. As shown by the appended chart (Chart XVI); theocin, theobromin sodium salicylate, caffein citrate, potassium citrate, and digitalis all failed to produce any diuresis, as shown by the twenty-four-hour amount of urine in relation to the fluid intake. It was thought possible that in this case the drugs might have produced an immediate diuresis which was offset by subsequent fall in excretion. To see whether or not this was the case, the patient's urine was collected in four-hour periods for fourteen days, but as shown by the chart (Chart XVII) there was no evidence of diuresis of this type

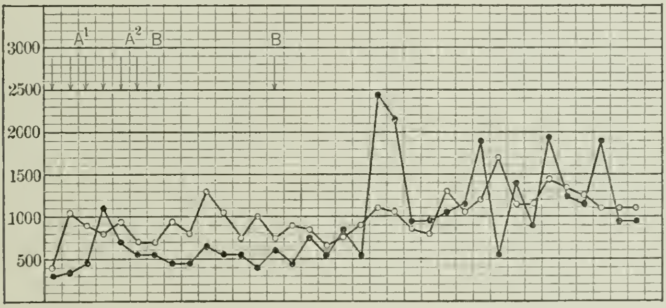

Chart XVIII.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under A^1 indicates a day on which the patient received three doses of 0.1 gm. each of powdered digitalis leaves; under A^2 a day on which the patient received two doses of 0.05 gm. each of powdered digitalis leaves. Each arrow under B indicates a dose of 0.3 gm. of theocin.

In another patient, aged thirty-eight years (Peter Bent Brigham Hospital, Medical No. 1754, Chart XVIII), single doses of theocin seemed to produce no effect. This patient came into the hospital on October 11 and remained until November 15. He noticed eleven days before coming in, that his legs began to swell, and five days before he came in that his face was swollen; two days before he came in the edema had involved his genitalia. This patient had a normal blood-pressure, signs of fluid in his thorax, possibly some fluid in his abdomen, and a marked degree of subcutaneous edema. When he came in his urine contained a large amount of albumin, many hyalin and granular casts, many of which had fat attached, but very few red blood cells. His excretion of phenolsulphonephthalein was 28 per cent. in two hours. His non-protein nitrogen was 36 mgm. per 100 c.c. of blood. During his stay in the hospital his blood nitrogen decreased to 24 mgm. per 100 c.c. of blood, and his phenolsulphonephthalein excretion increased to 39 per cent. The albumin in his urine decreased in amount and the casts decreased

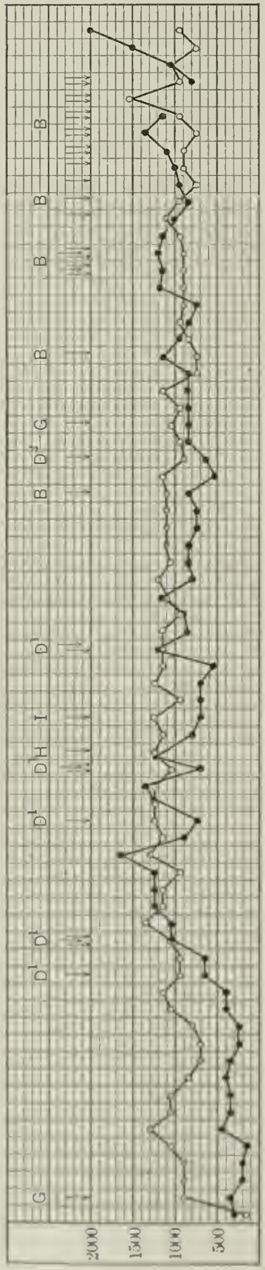

Chart XIX.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under B indicates a dose of 0.3 gm. of theocin; under D^1 a dose of 0.25 gm. of theobromin sodium salicylate; under D^2 a dose of 0.5 gm. of theobromin sodium salicylate; under G removing 2650 c.c. of ascitic fluid; under H 20 gm. of urea, and under I, 10 gm. of sodium chloride.

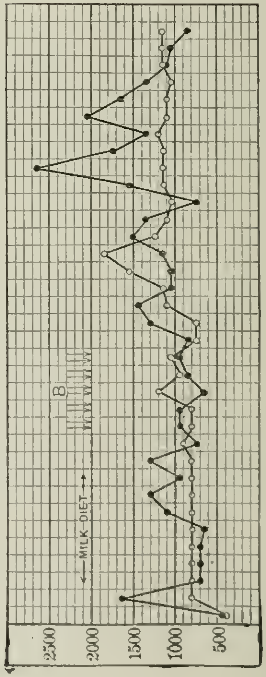

Chart XX.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under B indicates a dose of 0.3 gm. of theocin.

in numbers. Chart XVIII shows the lack of effect of digitalis and theocin and a subsequent diuresis on two days for which no cause could be assigned.

Another patient of similar type, aged thirty-one years (Peter Bent Brigham Hospital, Medical No. 1524, Chart XIX), was in the hospital from September 10 to November 18. Swelling of his legs developed about three and a half months before he came in. When he came to the hospital he showed considerable edema of his legs and trunk, with definite signs of fluid in his abdomen. His phenolsulphonephthalein excretion varied between 28 per cent. and 52 per cent. in two hours. His non-protein nitrogen was 23 mgm. per 100 c.c. of blood. His urine picture was essentially the same as in the preceding patient. His blood-pressure was 150 mm. of mercury. In this patient, as shown by the chart (Chart XIX), theobromin sodium salicylate and theocin each appeared to produce a slight though not constant diuresis.

A fourth patient, aged thirty-five years (Peter Bent Brigham Hospital, Medical No. 1879, Chart XX), was in the hospital from November 7 to December 12 with a history that three days before entrance his feet had begun to swell and he had some dyspnea. This was preceded about a week and a half before by nausea, with some vomiting. When he came into the hospital he had marked edema of his feet and lower legs with many coarse rales in his lungs. His blood-pressure varied between 140 and 190 mm. of mercury. His phenolsulphonephthalein output varied between 30 per cent. and 46 per cent. in two hours, and his blood nitrogen between 50 and 82.5 mgm. per 100 c.c. of blood. His urine showed a large trace of albumin, hyalin, and finely and coarsely granular casts.

On a diet of 800 c.c. of milk and no added fluid he had a moderate diuresis (Chart XX). He was then put on theocin, 0.3 gm. twice a day, from November 18 to November 22, during which period his diuresis was rather less than it had been previously. His edema had to a considerable extent disappeared. After theocin was stopped there was a slight temporary diuresis. Then on a larger intake of fluid slight edema developed. With a reduction in the fluid and the patient back in bed there was quite definite diuresis, as shown by the chart, though he received no drug treatment.

A fifth patient, aged forty-five years (Peter Bent Brigham Hospital, Medical No. 1885, Chart XXI), was in the hospital from November 9 to December 9, with a story that seven months before admission he had had pneumonia, and this had been accompanied by edema of his lower extremities, which a little later increased so that it involved his genitalia, and his abdomen began to swell. In another hospital this edema disappeared, but returned about four months ago shortly after discharge from that hospital. It remained small in amount, however, until about two weeks before admission to the Brigham Hospital, when it markedly increased. He also began to have nausea and vomiting. When he came into the hospital he had signs of ascites, edema of the legs, scrotum, and abdominal wall. His heart showed the physical signs of aortic and mitral insufficiency. His blood-pressure varied between 150 and 210 mm. of mercury. His phenolsulphonephthalein output varied between 22 per cent. and 33 per cent. in two hours, and his blood nitrogen between 37.5 and 39 mgm. per 100 c.c. of blood. His urine showed essentially the same picture as the preceding case.

When he first came into the hospital he was put on a diet of 800 c.c. of milk, with no added fluids. On November 15 he was put on a salt-free diet. On November 17 he was given 0.3 gm. of theocin twice, and on November 18 and November 19 he was given the same amount of theocin at 8 P.M. without any diuresis (Chart XXI). On November 22, 3700 c.c. of fluid were removed from his abdomen. Finally, on November 27, he was put on small doses of digitalis twice a day, with a definite diuresis.

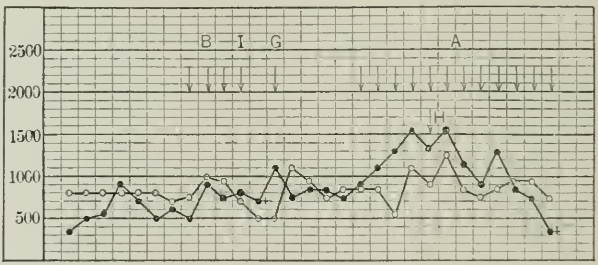

Chart XXI.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under A indicates a day on which the patient received two doses of 0.05 gm. of powdered digitalis leaves; under B a dose of 0.3 gm. of theocin; under G a day on which 3700 c.c. of ascitic fluid was removed; under H, 20 gm. of urea and under I, 10 gm. of sodium chloride.

That diuretic drugs are not always ineffectual is well shown by a cardiac case with aortic stenosis and insufficiency who was in the hospital from January 23 to March 21 (Peter Bent Brigham Hospital, Medical No. 2212, Charts XXII and XXIII) with marked edema. As shown by the chart (Chart XXII), theocin in connection with digitalis produced a marked diuresis, though theobromin sodium salicylate did not have the same result. With the theocin, however, he became markedly nauseated. It was thought that this difference in action might be due to differences in absorption of the two drugs. To determine this they were given intravenously at a later period during a second stay in the hospital and in the same relation to digitalis. The same difference in action was apparent after intravenous dosage; theocin produced a striking diuresis, as shown by the chart (Chart XXIII), while theobromin sodium salicylate produced a very slight increase in urine output.

Interestingly, nausea again occurred, though to a less extent, than when the drugs were given by mouth.

These several results seem to justify our skepticism in regard to the use of diuretics. Certainly more information is needed before we can employ diuretics efficiently in cases of renal or cardiorenal disease.

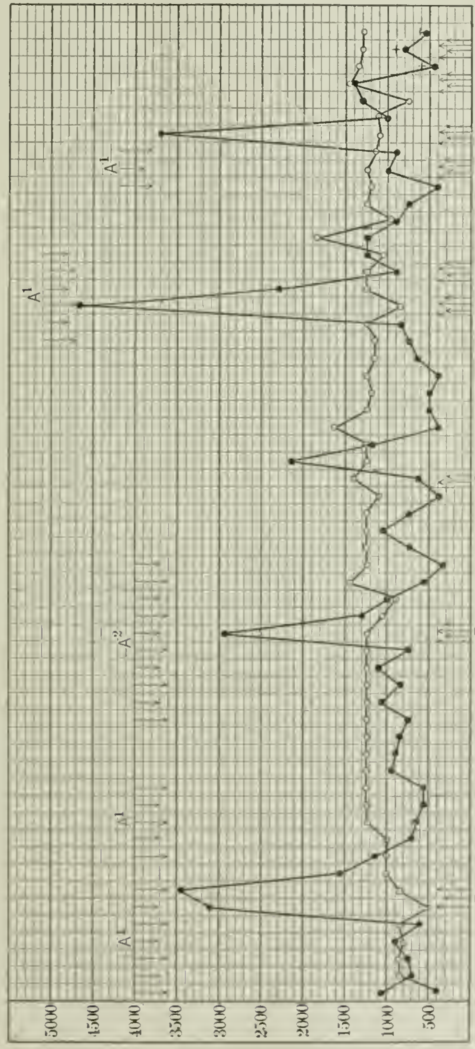

CHART XXII.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under A¹ indicates a day on which the patient received three doses of 10 c.c. each of an infusion of digitalis. Each arrow under A² indicates a day on which the patient received two doses of 10 c.c. each of an infusion of digitalis. Each arrow over B indicates one dose of 0.5 gm. of theocin. Each arrow over C indicates one dose of 0.2 gm. of caffein sodium benzoate. Each arrow over D indicates one dose of 0.3 gm. of theobromin sodium salicylate. Each arrow over E indicates one dose of 0.5 gm. of theocin sodium acetate.

D. FUNCTIONAL TESTS IN RELATION TO ANATOMICAL CHANGES IN THE KIDNEY. Up to the present time 18 cases of chronic nephritis have come to autopsy at the Brigham Hospital upon which enough clinical work had been done to make a comparison between the clinical and anatomical findings of interest. Most of these cases were seriously ill when they were admitted to the hospital, and consequently could not be put upon standard diets to which were added salt and urea to determine the relative ability of the kidney to excrete salt and nitrogen. Determinations of phenolsulphonephthalein excretion and estimations of the non-protein nitrogen in the blood were made, and, in addition, careful general clinical examinations were carried out.

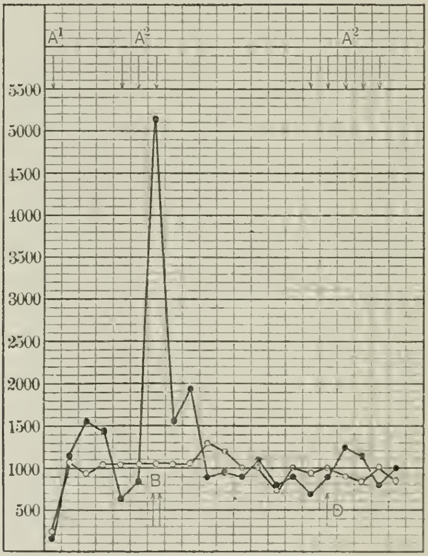

CHART XXIII.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. The arrow under A¹ indicates a subcutaneous dose of 1 c.c. of digipuratum and under A² a day on which the patient received three doses of 10 c.c. each of an infusion of digitalis. The arrows at B indicate two doses of 0.5 gm. each of theocin given intravenously and at D a dose of 1 gm. of theobromin sodium salicylate given intravenously.

In the 18 cases, microscopic study of the kidney showed a chronic vascular nephritis, in the sense used by Mallory in his recent book, in 14 cases, and in 4 cases the lesion was a chronic glomerular nephritis. The study of blood nitrogen, phenolsulphonephthalein excretion, and the excretion in the urine of albumin and casts did not give results during life which justified a definite diagnosis in the anatomical sense on many of these cases. In other words, during life it was not possible to accurately foretell what histological changes would be found in the kidneys in those patients who were studied in the last stages of a chronic nephritis. The clinical study of those cases has given much evidence of use in regard to prognosis. In a functional sense it has been possible to classify the cases into various groups, but it has not been possible to diagnose accurately the anatomical condition of the kidney. As has already been said, test renal meals and test diets could not be applied in these cases. Whether a more satisfactory anatomical diagnosis could have been made if these had been carried out is merely a matter of speculation.

It is hoped that as time goes on cases which we have studied in the earlier stages will return to the hospital for repeated examinations as their disease progresses, and in the last stages may be under observation. If autopsies can be obtained when such patients die, an opportunity will be afforded to compare the results of functional studies with end anatomical conditions. It is only in the earlier stages of the nephritis that satisfactory dietary studies can be made as well as other methods of estimating renal function. Until this happens it will not be possible to say how far an accurate anatomical diagnosis can be made during life. We feel sure that such functional studies as can be made in the late stages of chronic nephritis do not make possible an accurate anatomical diagnosis, because at this stage almost all parts of the renal function are at a low level of efficiency.

CONCLUSIONS.

A. TEST RENAL MEALS IN RELATION TO RENAL FUNCTION. 1. Of two general methods used the v. Monakow standard diet with days of added salt or urea and the Hedinger and Schlayer test day on a mixed diet, the first requires about ten days of hospital study and the second three days. Using the two methods on a series of patients we have obtained very similar results by each.

2. Though similar the results are not quantitatively identical. The same is true for the same test repeated several times on the same patient.

3. For the Hedinger and Schlayer test there is no constant normal curve of excretion. Normality consists in the ability to vary from period to period the amounts and concentration of the substances quantitated. Abnormality consists in a more or less marked degree of fixation in all of these values from period to period.

4. Fixation in excretion of nitrogen seems to develop at a later period in most cases than is true for water and salt.

B. QUANTITATIVE STUDIES OF NON-PROTEIN NITROGENOUS BODIES OF THE BLOOD. 1. Urea nitrogen in a series of cases averaged 63.4 per cent. of the total non-protein nitrogen of the blood, and its increase was usually proportionate to the increase of the total non-protein nitrogen.

2. Ammonia nitrogen increased slightly but not proportionately. The same held for uric acid and amino-acid nitrogen.

3. Creatinin showed roughly a proportionate increase.

4. The difference between determined forms of nitrogen and total non-protein nitrogen was greatest in cases with clinically most severe symptoms.

5. In the spinal fluid the increase in nitrogen is almost solely in urea nitrogen except in cases of anuria.

6. We can see no advantage in quantitating the nitrogen of the spinal fluid over quantitating it in the blood.

7. No relationship existed between the amount of non-protein nitrogen in the blood and changes in the retina.

C. DIURESIS IN RELATION TO DIURETICS. 1. Diuresis is relatively infrequent in the average hospital patient.

2. Except for diuresis in cardiac cases following digitalis, diuresis bears an inconstant relation to diuretic drugs.

3. In cases of nephritis with or without edema and without cardiac decompensation, diuretic drugs more often fail to produce a diuresis than the reverse.

4. In cardiorenal cases, diuretic drugs often produce a striking diuresis.

5. Our observations justify a healthy skepticism as to the efficacy of diuretic drugs in cases of nephritis without cardiac decompensation.

D. FUNCTIONAL TESTS IN RELATION TO ANATOMICAL CHANGES IN THE KIDNEY. 1. In 18 cases of chronic nephritis dying and coming to autopsy no constant relations have been found between anatomical lesions and renal function insofar as excretion of phenolsulphonephthalein, albumin in the urine, casts, presence or absence of edema, blood-pressure determinations, etc., are concerned.

STUDIES IN MONILIASIS OF THE DIGESTIVE TRACT IN PORTO RICO.[1]

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IN April, 1913, I wrote a paper[2] for the Tenth Annual Meeting of the American Society of Tropical Medicine, entitled "Notes on Sprue in Porto Rico, and the Results of Treatment by Yellowed Santonin," announcing the presence of that disease in the island. The paper was the outcome of a clinical study of 86 cases extending over some four years. While the disease, under the name of tropical scurvy or intestinal phthisis, has undoubtedly caused a formidable mortality for many years, of late, perhaps in the last decade, it has made startling advances and has now come to occupy a position in the very front rank of the serious and fatal affections of our island, especially dreaded by American residents, among whom it seems to be far more common and fatal than tuberculosis. That it is a disease caused by a specific organism seemed to me likely from the first. The paths most likely to lead to a recognition of that organism seemed: (1) A clinical investigation of the disease, and (2) an epidemiological survey of varied points on the island.

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[1] Read before the Association of American Physicians, May 11, 12 and 13, 1915, in Washington, D. C.

[2] Am. Jour. of Trop. Dis. and Prevent. Med., 1913, 1, 146.

Clinical experience with sprue from the early part of 1909, convinced me that, among other things, it was a separate and distinct clinical entity with four cardinal conditions, sore mouth, excessive intestinal fermentation, light, foamy diarrhea and a diminution in the size of the liver; that it was a chronic affection, with periods of relative health; that no specific had yet been found, nor was any medication comparable to a non-carbohydrate diet, santonin having been found wanting after long and persistent use, and discarded in 1913 for emetin, which suffered a like fate. In that year the Institute of Tropical Medicine and Hygiene made their annual expedition to the country districts of the interior and fixed the clinical laboratory, hospital and dispensary in a coffee plantation in the mountains of Utuado. We saw in open clinic for all diseases in a period of sixty working days, 10,140 persons, receiving over 36,000 visits. All physicians working with us were instructed to send cases not uncinariasis, as well as cases suffering from complications of that disease, to our special examining room, and as one of the diseases which we were especially seeking in our medical survey was sprue, it is not probable that many cases of it escaped our vigilance. Only 11 cases of complete sprue and 19 doubtful cases were seen, most of them from the town of Utuado. Thus the fact was disclosed that while occasionally found in the rural districts, sprue was really a disease of towns and cities, preferring to take its victims from the higher walks of life rather than from the less sanitary and apparently more exposed poor. For the purpose of contrast, let us consider 25 as the average minimum number of cases of sprue seen each year by physicians in San Juan who are on the watch for it. In this connection let it be said that among these physicians there is little contention over its tendency to present itself in family endemics.

Previously to this expedition, I had concluded that a likely source of infection was bread, rarely consumed by the country laborer, at best intermittently, and a staple in the home in towns. Porto Rican bread was in 1898–1903 a very savory food. Its peculiarly pleasant taste and European style of confection, accredited it to every table. But the bread of Porto Rico has degenerated much in flavor and in confection in the last ten years, complaints of its sourness and soddenness have become more and more frequent, and coincident with this deterioration intestinal fermentative conditions have increased.

Bahr's[3] "Researches on Sprue" was discouragingly received by some of his colleagues, who replied to his modest statement that the circumstantial evidence pointed to *Monilia albicans* as being the cause of the disease by expressing their inability to accept as a causal agent a fungus common in England where sprue is unknown. At that time I had under my care one of the most typical and, considering the sanitary excellence of his house, one of the most disquieting cases of sprue to American residents which had up to that time claimed public attention. The patient, a young government official, gradually reached the stage of marasmic toxemia, in spite of drugs, trips to the North, and even the classical diet. I sent him North after a partially successful dietetic regime extending over three or four months, and in New York the same diagnosis was independently made by Dr. Crow, U. S. N., who had seen sprue in the East. His return coinciding with the newer ideas of the etiology of sprue, I made three unsuccessful attempts to obtain a growth of yeasts from the denuded but non-inflamed tongue. One day, however, in the midst of an attack of sore tongue, a growth was obtained by scraping, and this culture, together with three others, two of which were cases of tongue sprue in children, formed the basis for a preliminary note[4] entitled "A Monilia Found in Certain Cases of Sprue."

From that time to the present I have made 240 cultures from the tongue, and 50 from the feces in 197 persons, all my own patients and all under my constant observation save five. I divided my sources of culture into three groups: (1) Cases of clinical sprue. (2) Cases with symptoms indicating involvement of the digestive tract, chiefly of a fermentative nature ("gastric and intestinal dyspepsia," etc.), or those presenting a simple stomatitis. The clinical picture of sprue lacked clearness in this group. Herein are included cases entirely cured of a past typical sprue. (3) Cases surely not sprue, and bereft of past or present history of disease of the digestive tract.

The first group consisted of 49 cases; 27 presented a clear picture with the four cardinal symptoms of complete sprue at the time of examination, and an actively inflamed and typical sprue tongue; 20 were cases of the intestinal type at the time cultures were made, but 7 gave histories of having had the complete picture previously; 2 were cases of tongue sprue, but also gave previous histories of the complete type.

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[3] Trans. Soc. Trop. Med. and Hyg., April, 1914, vii, No. 5.

[4] Jour. Am. Med. Assoc., 1915, xiv, 810.

All were promptly positive for monilia. Forty gave the cultural characteristics of the new monilia only and the remaining 9, apparently identical on Sabouraud's glucose agar, have not yet been grown in the required media. This gives a percentage of 100 for this group positive for monilia, all probably identical with the new species.

The second group consists of 82 cases. There are many in which no justification for a suspicion of sprue exists, but they are retained in this group because they give past or present histories of gastrointestinal disturbance. They may be subdivided as follows: (1) Cases whose histories are suggestive of sprue, and in whom some symptoms still exist. These histories do not, however, justify a positive diagnosis. There are 19 in this subdivision. One gave a positive culture for the new species. Four gave monilias of type entirely distinct from mine, and in 3 of these cases the diagnosis of pellagra was pending. In one of these it has been positively confirmed. Five are frank cases of pellagra now, and all were negative for monilia after repeated search. (2) Cases with a history of gastrointestinal vagaries in which the dominant note is usually "fermentative dyspepsia." There are 29 in this subdivision: 14 were positive for monilia, 7 for my species and 7 clearly not mine. (3) Cases with inflamed tongue alone. There are three such cases, all negative for monilia. (4) Cases giving a clear history of past sprue generally some years back. There were 20 of these, and all were negative for monilia. (5) Five cases with a colorless history, or a history not diagnostic of sprue, which I failed to see as cultures were made and sent in by colleagues. All were negative for monilia. (6) Six cases with good histories of sprue awaiting confirmation by cultures. The preliminary plate cultures were mature at the time of my leaving San Juan. All seem to be of the type to which the new species belongs.

Twenty-five, therefore, of the 82 cases in this group yielded monilia on culture, but only 14 belonged to the new species, a percentage of 17 for the new species.

The third group consists of 66 cases. No one of these presented any symptoms of sprue, and many were apparently healthy in all respects. Four yielded monilia; two positive for the new species, the other two being entirely at variance therewith. The rest were negative for monilia, giving a percentage of three in this group for the new species. Animal experimentation will be detailed when completed.

The laboratory study of sprue has been limited to the working out of cultures, and this, naturally, has consumed much time, especially when one considers that all of the steps from the making of media, to titration, from collection of pathological specimens, to their cutting, mounting and staining, has with negligible exceptions, been done personally by the writer. Nevertheless, a few remarks may be made on the subject of animal experimentation.

Small laboratory animals are susceptible to inoculation by the new species, usually dying of a general mycosis in a few days if the monilia has not had its virulence weakened by age or too frequent transplanting. A large Belgian hare received a few drops of a ten-day culture of the monilia, recovered from the patient mentioned in the forepart of this paper, by hypodermic injection into the muscles of the tongue. Death occurred from general mycosis in seventy-five hours, and the necropsy cultures were made from liver, spleen, kidney, lung, heart's blood, and the muscles of the tongue. These cultures resulted directly pure for the new species in twenty-four hours. An interesting side-light is thrown by the morbid anatomy of this hare upon the statement of most writers who have had the good fortune to autopsy cases of sprue, as the mucous membrane of the bowel was found to be coated with a white, grumous layer. Owing to the leaking of the syringe, the animal had received by the mouth from 1 to 2 grams of the culture, and upon examining the stomach and small bowel they were found heavily lined with a white, creamy coating, examination of which demonstrated the immense preponderance of yeasts. To this it should be added that this animal, distinct from rats and guinea-pigs intraperitoneally injected, had a sharp diarrhea and an enormous production of gas before death.

Intraperitoneally, two white rats were injected, one with a glucose bouillon culture of the new species recovered from another American, who like the first died of the disease; the other with a similar culture from the daughter of a physician dangerously ill of sprue in the stage of marasmic toxemia. Both animals died of general mycosis, and from both, pure cultures were directly recovered from all the principal organs.

A hare which had proved himself resistant to the intraperitoneal injection of an old culture of the monilia, which promptly killed the first animal, received in the tissues of the ear 4 grams of a bouillon culture, and three weeks later it was found that the entire organ was the seat of a "blastomycotic" ulcer.

Feeding experiments, however, have been disappointing, although not yet persistently and systematically worked out. A guinea-pig of about 1000 grams was fed the new species in pure culture mixed with malted milk, it having been previously fed throughout a period of ten days with malted milk alone. Diarrhea and gaseous distention were produced, and after three weeks the animal died. The histopathological picture has not been worked out, but cultures from the organs were negative, save from mouth and stomach, which were positive for the new species and from the spleen. which gave a culture apparently unlike the new species.

A monkey similarly fed, became weak, morose, and emaciated, with sharp diarrhea, and the predominating organism in his stool is a yeast which in culture proved to be the new species of monilia.

In all feeding experiments, one should bear in mind that we are dealing with an organism of confessedly low virulence, and much patient and careful work must be done to elicit results worth citing as confirmatory.

The original technic of Wassermann was applied to the complement-fixation test for cases of sprue by Gonzalez Martinez, of our Institute of Tropical Medicine, just as I was leaving the island for the United States. I selected three strains of the new species from among my cases, and an antigen was prepared from these. Twelve cases not sprue were negative, and four clinically and mycologically sprue were positive. It is interesting to add that since that time all cases not sprue, and awaiting the Wassermann reaction for syphilis, are subjected to the complement-fixation test for sprue and are so far all negative.

Monilia, Species Undetermined. The organism is a typical monilia reproducing by side-buds and terminal conidia from specialized hyphæ, as well as by budding from yeast forms. Ascospores are never seen, but chlamydospore-like bodies are frequent, especially in older cultures. The yeast is round, from 2 to 7 microns in diameter, averaging from 3 to 4, with clear, clean-cut outline, usually containing a relatively large refractile body, and a much larger, faintly outlined vacuole. Tendency to mycelial formation is seen by the round yeasts enlarging and becoming oval. As the yeasts become larger, many active, highly refractive bodies of the size of a staphylococcus race incessantly about within the organism, reaching their largest number and greatest size in the chlamydospore-like, thick-shelled forms and frequently passing out into the fluid medium in which they grow, thus confusing the novice into believing that a contaminating coccus may complicate his apparently pure culture.

The mycelium is well developed, usually very abundant and presenting sparsely branching hyphæ, sometimes over a 1000 micra long which consist of articles from 10 to 60 micra long by 1.5 micra broad, the usual length being 15 micra. These hyphæ are of two distinct varieties; thin, often granular and 1 to 1.5 micra wide, and thick, often clear and 2.25 to 3 or 4 micra wide. The latter variety, at times without apparent structure interiorly, is more frequently punctuated at regular intervals by the highly refractile bodies described in the round and oval yeasts. These are from $\frac{1}{2}$ to 2 micra in diameter and give a brilliant beaded appearance to the article. They stain as for chromatin by Giemsa. At times with the refractile bodies, at times without them, articles are seen frequently to have rectangular vacuoles of the same refractive index as though seen in the larger yeasts, thus dividing the article as it were into compartments and giving the hyphæ the appearance of a bamboo pole sawn longitudinally. In old culture many large yeasts are seen of 10 to 13 micra diameter as also involution forms of bizarre and clumsy outline, empty, collapsed chlamydospore-like bodies and heavy shelled prickle cells faintly suggesting the ova of ascaris lumbricoides.

Staining Reactions. The best class of stains for this organism belongs to the Romanowsky series. I personally prefer staining overnight in a weak Giemsa as by it the nuclear elements come out beautifully. The only satisfactory stain I have yet found for the outer shell of the mycelial threads is by Bodin's Victoria blue method. For staining in tissues there are only two methods that can be recommended and they are both of the highest excellence. The first is Weigert's fibrin method giving fine contrast by Gram's application. The second is Bodin's Victoria blue method. This may be summarized as follows: (1) Paraffin sections of mercuric chloride, absolute alcohol or formalin fixed tissue sections not over 5 micra; (2) after usual preparation for staining immerse for five minutes in a 1 per cent. erythrosin, aqueous solution. Wash well; (3) twenty-four hours in equal parts of a saturated alcoholic solution of Victoria blue and distilled water; (4) thorough washing in water and Weigert's stronger Gram solution for five minutes; (5) thorough drying and differentiation in aniline oil and xylol, equal parts; (6) thorough washing and clearing in xylol; (7) mount in balsam.

CULTURAL PECULIARITIES. The first labor was that of finding a specific medium. That one has been found in Sabouraud's glucose agar, 4 per cent. +2, is evident to anyone who cares to try it. As far as these yeasts are concerned it is ideal, as bacterial growth is efficiently inhibited even in strokes from feces and agar plates, the monilia standing out with unfailing precision as moist, white colonies of sharply contoured lines.

In culture from the tongue, a section lifter is sterilized in the flame and the borders and tip are gently scraped, the grumous material being spread upon a Sabouraud glucose agar slant by means of a sterile platinum loop. Twenty-four to forty-eight hours is all that is usually needed to bring out a monilia which is plated by the familiar three-plate method, and is easily recovered in another twenty-four to forty-eight hours in pure culture. For feces the Sabouraud agar is poured into a Petri dish, allowed to cool and harden, and is infected by parallel strokes. Suspicious colonies are then plated by the three-plate method. These methods were strictly observed in all cultures except that two, instead of three plates were frequently used.

The following media were employed in studying the species under consideration: Plain agar, glucose-, maltose-, levulose-, saccharose-, galactose-, lactose-, mannite-, dextrin-, erythrite-, raffinose-, dulcite-, isodulcite-, inulin-, and nutrose-agars. Loeffler's blood-serum mixture and plain blood serum; potato, plain and glycerinized; carrot, plain and glycerinized; plain gelatin, 20 per cent. +1;

plain and litmus milk; beer wort; Dunham's peptone solution; ox bile; plain bouillon, sugar-free bouillon; glucose-, maltose-, levulose-, saccharose-, lactose-, and mannite-, bouillons at 2 per cent. +1 and galactose-, dulcite-, dextrin-, raffinose-, arabinose-, inulin-, erythrite-, amygdalin-, asparagin and isodulcite at 1 per cent. +1.

The first four strains and several others later in the series were sown in all of these media and carefully checked upon as follows:

All cultures were run for at least two weeks and daily notes taken of each before deductions were made. Before final conclusions were reached the purity of the culture was tested. Solid media were allowed to run several months, especially gelatin cultures. All media were carefully titrated, as a rule to +1 by the rules of standardization of media recommended by the Bacteriological Committee of the American Public Health Association. Incubation was practiced at 33° to 35° without rubber tops to the tubes, these conditions being apparently most favorable to the growth of this monilia.

For fermentation tests, each culture in any sugar medium consisted of a fermentation tube, its control tube for final titration, and a litmus tube and its control to demonstrate daily progress in changing reactions. Incidentally it may be remarked that without titration by some such standardizing method as the one named above before sowing and at the close of the fermentation test, conclusions are greatly invalidated, as important and delicate reactions are quite missed. All sugar media were sterilized at the temperature of flowing steam for from ten to fifteen minutes on each of three successive days. Autoclaving splits the sugars. At the close of the period required for a complete fermentation test, the uninoculated media, which had been incubated along with the rest, was first titrated; then the inoculated media. Titration was performed in each case both hot and cold and the results recorded. The varying daily gas production was recorded as was the daily reaction in the corresponding litmus bouillon.

The monilia in question was found to prefer an acid, although it will grow well in alkaline media. Its adaptability is further shown in that on every medium tried it grew without difficulty, but it flourishes most luxuriantly on glucose, levulose, maltose, saccharose, galactose, and carrot.

The characteristics of the organism are best elicited by Sabouraud's glucose agar, carrot, blood serum, plain gelatin, litmus milk, and by fermentation tests in glucose, levulose, maltose, and saccharose bouillon (2 per cent. +1) and galactose bouillon 1 per cent. +1.

On Sabouraud's agar in from twenty-four to forty-eight hours a clean-cut, round, hemispherical, smooth, creamy white, moist, refractive colony is produced of the consistence of thick cream.

Small colonies are very beautiful under the lower power seeming to be like silvered mosaic. Later they tend to become acuminated in the centre and rapidly run together to form a thick cream all over the agar. They give off a yeasty smell and remind me of some Porto Rican bread and the stools of my cases. A young culture on solid media is not given to the production of mycelium but in the water of condensation it is abundant. Later the smooth creamy layer in some media, often apparently due to a mere bagatelle of half a per cent's difference in acidity of the original media, becomes knarled and twisted like a bunch of worms or the roots of a vine—or even like a delicate honeycomb.

The growth on carrot is distinguished by its tendency to rise high and stick rather closely to the line of plant, giving the appearance of heavy bits of raised embroidery. On blood serum a fine, not raised, at times almost invisible layer is made out. No liquefaction nor decolorization takes place. The growth in gelatin is remarkably faithful to type. It does not liquefy the media, stabs showing a limited round growth on the surface and fine hair-like lateral shoots all the way down to the lower extremity giving the appearance of a test-tube cleaning brush.

Milk is not coagulated and litmus milk grows steadily more and more alkaline. There is no period of acidity nor decolorization.

In discussing the sugar tests I shall have to take issue with the eminent authors whose versatility has enabled us to make use of these valuable but much over-rated means of differentiating species. Whether these gentlemen used our exact American methods of titration is open to speculation. They do not say that they did but I suspect that they did not. Had they done so perhaps Castellani and Chalmers would not offer such a bewildering series of "species" of monilia to the interested reader.

Such "species" as are to be depended upon not to produce gas when they are supposed to produce acid alone in a certain sugar bouillon, especially when they furiously ferment glucose, maltose and levulose, do not seem to me good. For one thing stands out quite clearly in these sugar tests: If a monilia produces acid, it is likely to produce gas, sooner or later. I have sown strain IV on one occasion and produced acid and gas in glucose, maltose and levulose; acid alone in saccharose and galactose. Two weeks later I have sown the same monilia, not from the culture on sugar media, possibly by that time educated to ferment sugars, but from the original source of the first culture. The result of this re-sowing was gas and acid in saccharose and galactose, as well as in the first three.

The species must not therefore be lightly made on sugar tests alone, when solid media, morphology and hanging drop specimens, not to mention inoculation results in animals, complement fixation tests, etc., speak for unity. In general, however, sugar tests are a wonderful help if one will only remember that a lively acid and gas producer in glucose, levulose and maltose will often do likewise in saccharose and galactose.

The species under consideration brings about a reaction tending toward alkalinity in all other sugar-media, with the possible exception that mannite and dextrin are apt to remain unchanged. Plain and sugar-free bouillon lose also in acidity. The characteristic of this monilia in bouillon is to leave the media clear, even after very long growth, with a more or less abundant sediment at the bottom of the tube. The growth at the surface varies, being almost nil if the organism does not grow vigorously in the particular media, very heavy if it does. Heavy growths at the surface produce a pellicle with a thick collar at the circumference which in the process of evaporation of the liquid is drawn out into a belt around the inside of the tube. Later this pellicle falls to the bottom and a new one takes its place. The superficial growth is more apt to have a predominance of mycelium, the sediment an excess of yeasts.

Conclusions. Bahr's evidence in favor of regarding sprue as a "blastomycotic" infection is as follows:

1. Yeast cells and mycelial elements are found intracellulary in scrapings of the tongue lesions at an early stage of the disease, but cannot be found at a later stage in scrapings of the same structure when inflammatory symptoms have subsided.

2. Yeasts are the only organisms found in the deep layers of the tongue in microscopic sections; the evidence that this infection is not one of recent date receives support from the chronic inflammatory changes in the corium of the papillæ, and from the presence of Russell's bodies in this situation.

3. The desquamation of the epithelial cells, accompanied by subacute inflammation of the tongue and of the esophagus, are changes such as would be expected from a study of the mode of growth of the thrush fungus and of its low order of virulence.

4. A general infection of the intestinal mucus with yeasts was found in sprue post-mortems, but no such a general infection in 26 cases of other chronic wasting diarrheas.

5. The stools of sprue, their frothy and gaseous character, are such as one would expect in a blastomycotic infection of the intestinal canal.

6. The relapsing nature, the chronicity and latency of the disease, are compatible with what is known of the life history of the blastomyces, their periods of attenuated growth and powers of sudden recrudescence.

7. There is no evidence in favor of regarding the sprue yeast fungus as being otherwise than identical with the thrush fungus (Monilia albicans), an organism possessing a very low pathogenic power, but it is possible that under certain conditions, as for instance

in the tropics, this power may be greatly augmented. In support of this view I may add that it is a well-recognized fact that there are numerous varieties of yeasts employed in brewing beer and in making wine, and the predominance of one variety in certain districts imparts to the local wine its characteristic flavor, which, though differing widely from each other in their powers of growth and fermentation, yet resemble each other minutely in their morphological and cultural character. May it not be that their pathogenic as well as their other properties, are capable of being influenced by local conditions?

8. Wasting and anemia, both symptoms of sprue, can be produced by continuous intravenous injections of small doses of broth cultures of a pathogenic yeast; moreover, a degeneration of the hepatic capillary endothelium, apparently similar to that found in the sprue spleen, may be produced in these animals by the same means.

9. Diarrhea, atrophy of the lingual papillæ as in sprue, digestive disturbance, and an aphthous ulceration of the mouth are commonly found in infants, the subjects of thrush infections in temperate zones.

10. It is possible that obscure diseases of the alimentary canal in children in temperate zones, such as Gee's celiac diarrhea, are of the same nature as sprue in adults in the tropics. A hypothesis of this sort would explain the occurrence of sporadic cases of sprue in temperate zones.

11. The local affection of different portions of the digestive tract with this fungus would best explain the varying clinical manifestations of sprue.

12. To maintain such a hypothesis it is necessary to stipulate for a third factor, a predisposing cause, which may exist in the local tropical climatic conditions, which favor a more precocious and luxuriant growth of all fungi, a matter of common observation to all laboratory workers in the tropics.

I am able to fully corroborate Bahr's evidence in all save human necropsy findings, as yet denied me, and with the exception of his statement that the sprue yeast fungus bears no evidence of being otherwise than identical with monilia albicans. In this matter we are not in accord as far as it may apply to Porto Rico where I have described a species, not *monilia albicans*, present in 100 per cent. of my cases of clinically positive sprue. In addition to this I have isolated this new species from the centre of a loaf of bread from an endemic focus in Porto Rico.

I therefore offer the following tentative conclusions drawn from the work as studied in Porto Rico and described in the body of this paper and from the accepted facts presented by authors regarding the human histo-pathology.

CONCLUSIONS. (*a*) *Clinical:*

1. Sprue is usually a mild disease with a veiled picture in which intestinal fermentation is usually present, a tendency to spontaneous cure and a ready submissiveness to a non-carbohydrate diet.
2. Tongue lesions are often clinically and histo-pathologically indistinguishable from ordinary thrush, a disease due as a rule to monilia albicans.
3. Clinically and histo-pathologically the picture of the tongue is projected on through stomach to intestine.
4. Chronic intoxication supervenes after well-developed sprue, and the liver atrophies without cirrhotic changes, secondary anemia making its appearance.
5. The intestinal lesions produce large, acid, frothy, white stools with excessive gas production, and full of yeasts. The character of these stools does not warrant the belief that serious ulceration takes place.
6. There is a tendency to chronicity and to periods of latency in which decided betterment or apparent cure may take place.
7. Drugs are of little avail save when used symptomatically for definite clinical crises and no specific has yet been found.

(*b*) *Epidemiological:*

1. Sprue is a disease of towns and cities where bread is a staple food.
2. Sprue is apparently rare in the country districts where bread is not at least a daily food and where often it is eaten only at long intervals.
3. Family endemics are noticeable.
4. There seems to be a racial predisposition to sprue in persons of northern birth.

(*c*) *Biological:*

1. A monilia, not heretofore described, and of undetermined species is apparently constantly found in cultures from the inflamed tongue or feces of persons suffering from sprue in Porto Rico.
2. This monilia has been found in the centre of a cooked loaf of bread baked in an endemic zone.
3. This monilia has been found in certain cases of fermentative disturbance of the intestine in which the complete picture of sprue is not developed.
4. The monilia is found in only 3 per cent. of persons, apparently entirely healthy or, at least, free from any gastro-intestinal disturbance.
5. The complement fixation test is positive for all of the reduced number of cases of complete sprue in which it has thus far been applied and negative for several times that number of persons without sprue.

6. This monilia is not only productive of mycotic septicemia in small laboratory animals injected with virulent culture but will produce severe and intractable mycotic ulcers in their tissues when they are relatively immunized to the extent of preventing a mycotic septicemia.

THE OCCURRENCE OF SPRUE IN THE UNITED STATES.[1]

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Tropical sprue, or psilosis, was probably first referred to in American literature in the writings of Dr. John Brickell,[2] a Dublin physician, who was an emissary of the Crown to the Cherokee Indians early in the eighteenth century. In his report he discusses the diseases of the colony of North Carolina, and in addition to yaws he mentions "white flux," which, in all probability, was the disease described in 1776 by Hillary, in Barbadoes, as sprue. The identity of this West Indian sprue was never questioned by Sir Patrick Manson,[3] though Carnegie Brown[4] still contends that true sprue is limited in its distribution to tropical and subtropical eastern Asia. Fortunately for us many of our medical men, especially of the Army Medical Corps, became familiar with true sprue in the Philippines, and not only brought back with them this intimate acquaintance, but were able to identify the disease known as sprue in Porto Rico as true sprue of the East. In recent years many observers have suspected that sprue existed in the United States, but only in the last decade has anyone had the temerity to actually make the diagnosis except in cases invalided from the tropics. The return of missionaries from China and Ceylon suffering from sprue has given us many opportunities to become familiar with true Eastern sprue and to compare it with the milder type of sprue in the Southern States.

In 1905 St. J. B. Graham,[5] of Savannah, reported four cases of sprue which had originated in Georgia. This observation was based on experience in the Philippines, and the correctness of the diagnosis can hardly be questioned.

In 1907 H. F. Harris,[6] of Atlanta, reported a number of cases of sprue. Later in that same year Searcy, of Alabama, reported the existence of pellagra, and Harris concluded that he had confused the two diseases; but a perusal of his careful report will convince anyone that at least some of his cases were sprue, and it is not improbable that his cases of pellagra were complicated by sprue. In a recent personal communication, Dr. Harris says there exist in Georgia cases which exactly correspond to tropical sprue of the East.

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[1] Presented at the meeting of the Association of American Physicians, in Washington, May 13, 1915.

[2] The Natural History of North Carolina, Dublin, 1737. Reprinted by the State Library of North Carolina.

[3] Tropical Diseases.

[4] Sprue, William Wood & Co., New York, 1908.

[5] Georgia Practitioner, August 15, 1905, xi.

[6] Tropical Sprue, Report of the Georgia State Board of Health, 1907.

In 1909 R. Hessler,[7] of Logansport, Indiana, published an article on sprue, but his experience seems to have been limited to cases invalided from the tropics. In 1911 J. K. Simon,[8] of New Orleans, reported a probable case of sprue.

In 1912[9] I called attention to the existence of sprue in the United States in connection with the recognition of pellagra. The two diseases are greatly confused, for reasons to be mentioned later.

At the last session of the American Medical Association, Hiatt and Allan[10] reported a number of cases of true sprue. Some of the cases were invalided from Porto Rico, but in one instance, at least, the case originated in North Carolina and the victim had never been out of the state. The most valuable feature of this article is the comparison of the disease brought in from the tropics and the disease as it occurs in this country. These observers have had the opportunity to study the disease from the two sources, and their conclusions are most important in settling this disputed point.

At the School of Tropical Medicine of Tulane University no case has yet been observed which originated in the United States, though quite a number from the West Indies have been studied. Notably among the latter is an unpublished case of Dr. Allan Eustis, with an autopsy by Dr. C. W. Duval. The case came from the Charity Hospital in New Orleans.

The place occupied by tropical sprue in medicine at this time is most unsettled. Manson, Cantile, Begg, P. H. Bahr, and many others, especially of the English observers, count it a definite disease entity, while W. E. Musgrave and T. W. Jackson consider it a condition or state which may occur in conjunction with or as a complication of many of the diarrheal diseases of warm climates. This latter position is chiefly justified by the great variability in the descriptions of the various writers. Any condition attended with stomatitis and diarrhea has at one time or another been diagnosed sprue. Such a state of things is most unfortunate, and will probably not be corrected until the causative agent of sprue is definitely determined. Faulty use of synonyms has added greatly to the unsettled place of sprue in medicine. This is well illustrated in the use of hill diarrhea as a synonym when a number of observers are quite emphatic that this disease and sprue are not related in any sense. Manson gives in his list of the synonyms of sprue, Cochin-China diarrhea, while Dr. C. W. Stiles, in a personal communication, says that medical zoölogists understand by this term an infection with the Strongyloides stercoralis. This infection was found by Dr. Stiles in a number of the Southern States, with a distribution almost identical with that of uncinariasis.

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[7] Jour. Indiana State Med. Assn., April, 1909.

[8] South. Med. Jour., July, 1911.

[9] A Treatise on Pellagra, 1912, Appleton & Co., New York.

[10] Jour. Amer. Med. Assn., 1914, lxiii.

Leonard Rogers,[11] in discussing the results obtained by him in the treatment of sprue in Calcutta with emetin and a streptococcal vaccine, remarks that the vaccine effect was quite striking, and in explaining it adds, "We should bear in mind that sprue is a purely clinical term, and there may be more than one causative agent, just as in the case of dysentery."

The term sprue has been adopted in the nomenclature of diseases of the Royal College of Physicians. The word was borrowed by Manson from the Dutch word "spruw," which was used in Java to designate the disease. If the original description of Manson is followed closely there need hardly arise confusion from the use of the term. Unfortunately the word has been so loosely used that it has tended to justify the position of those who contend that there is no such disease.

W. E. Musgrave[12] proves one of the most convincing advocates of the view that sprue is merely a condition or state which may occur in various intestinal infections. In spite of this in one of his cases no parasitic cause was found, and the case must be regarded as sprue.

Mayo Robson[13] found that in many cases in which the diagnosis of sprue had been made, the condition was really a pancreatic disturbance of an inflammatory type, and that in other cases pancreatic involvement formed an important complication. In this connection it is interesting to note that Musgrave in one case noted that the pancreas was small and presented a dark, muddy appearance, but without areas of hemorrhage or necrosis. In another of his cases the pancreas was pale and firm. In Eustis's case the autopsy notes by Duval mention a resistance on cutting indicative of interstital changes of the pancreas. It seems probable that some cases of chronic pancreatitis have been confused with sprue or that in sprue the pancreas plays an important role. It is obvious that much study is needed to clear up the question of the possible relationship of the pancreas to sprue, and that this work must be along the lines of histological study of the pancreas and of pancreatic functional tests.

According to the original description of sprue by Manson there

[11] Two Cases of Sprue Treated by Mouth Streptococcal Vaccines and Emetin Hydrochloride Hypodermically, Lancet, June 6, 1914.

[12] Sprue, or Psilosis, in Manila, Amer. Med., March 8, 1902.

[13] British Med. Jour., July 27, 1907.

is a definite symptomatology which should save much of the present unnecessary confusion. It is a chronic disease occurring in the tropics and in certain subtropical sections which is characterized chiefly by a peculiar type of diarrhea, by stomatitis, by decrease in the size of the liver, and by marked secondary anemia. There is a tendency to frequent recurrences and the downward course. The diarrhea occurs chiefly in the morning hours, and is unattended by tenesmus, blood, or mucus. The movements are semiliquid, though at times more nearly liquid, acid in reaction, and contain much gas. The odor is regarded as peculiarly foul. The color is light, due to a colorless reduction product of hydrobilirubin known as leukobilirubin. In addition to this the large amount of fat in the stool contributes to the light color. The size of the stool is a notable point, one which was emphasized by the late J. H. Musser as a valuable sign in pancreatic disease. In addition to the failure in the absorption of fats it is generally claimed there is a defective carbohydrate digestion. P. H. Bahr[14] found in his Ceylon cases that the fat absorption varied from 70 to 90 per cent., and that there was a complete absence of all pancreatic ferments. In a case of sprue from Porto Rico, Pratt and Spooner[15] found in addition to the intestinal disturbance pancreatic insufficiency which was indicated by the Einhorn-Schmidt thymus test and the Sahli glutoid capsule. The absorption test showed a fat loss of 45 per cent. and a nitrogen loss of 15 per cent. Though the stools were light in color there was a definite reaction for hydrobilirubin by the Schmidt test. The stools were yellow and voluminous, and contained many oil droplets as well as crystals and flakes of fat. It will be noted that these observers found a much greater fat loss than did Bahr. In a recent personal communication, Dr. Pratt mentions a case of sprue without pancreatic insufficiency in which the fat loss was found to be 59 per cent. He thinks that in this case the intestinal lesion is probably responsible for the condition.

The reduction in the size of the liver is not distinctive of sprue, as it occurs in other like conditions, as, for example, pellagra. It is the result of the general condition of malnutrition. Likewise, the anemia and marked prostration are of no particular significance from the diagnostic standpoint.

Sir Lauder Brunton[16] makes small mention of the shrinkage of the liver or the type of diarrhea, but lays particular stress on the aphthous stomatitis. Unfortunately, there is as much diversity in the description of the mouth symptoms as of the character of the feces. The original account of Manson is the most accurate, and should be followed. He recognizes definite stages through which the inflammatory process passes. In the beginning there is simple hyperemia, which is followed by denudation of the epithelium, and this, in turn, is followed by the formation of minute herpetic vesicles which occur singly or in groups, and are surrounded by inflammatory areolæ. The vesicles rupture, leaving small, superficial erosions which are very painful. Congestion and swelling of the fungiform papillæ, particularly about the tip and edges of the tongue as well as superficial cracks on the dorsum, are also mentioned. From this account of Manson the various writers have departed in varying degree. Most writers are content if there is glossitis or esophagitis to pass over the further consideration of the degree or kind of process and count it a positive symptom. Because of this lack of accuracy there is great confusion with a number of conditions, but chiefly with pellagra. It is to be recalled that in pellagra, as a rule, there does not occur definite ulceration, though Crombie's molar ulcer has been noted by H. F. Harris. There is no reference in sprue literature to salivation, which is so conspicuous a symptom in pellagra. The pain from glossitis, pharyngitis, and esophagitis is much more acute in pellagra than in sprue.

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[14] Soc. Trop. Med. and Hyg., London, 1911.

[15] Jour. Amer. Med. Assn., lix, No. 3.

[16] Edinburgh Med. Jour., 1900.

W. Allan[17] has called attention to the marked similarity of the symptoms of amebic dysentery and pellagra when the skin eruption of the latter is absent. This same warning should be mentioned in connection with the differentiation of amebic dysentery and sprue. This difficulty is made the greater by the fact that sprue may complicate amebic dysentery. In amebic dysentery the simple fact of the occurrence of stomatitis and diarrhea (the two symptoms so often counted sufficient for a diagnosis of sprue) will lead to error without a study of the feces.

The disease most frequently confused with sprue is pellagra, and it is this fact which justifies this report. There is so much similarity in a portion of the disease picture of sprue that some writers, notably J. Burnet,[18] of Edinburgh, and C. E. Stewart[19] argue that the two are in reality one and the same.

In the United States the diagnosis of pellagra in the absence of skin lesions is made with considerable possibility of error. It may be that in those countries where the disease has occurred for a much longer period, the medical profession has acquired more skill in its recognition, basing their opinions on signs other than the skin manifestations. For the present, at least, we are not justified in making such a diagnosis without skin lesions unless the history of a past outbreak is quite definite. In reviewing my cases, which began in 1905 and include several hundred, I find that at the time of examination the skin lesions were wanting in a large number, and a note is made leaving doubt as to the correctness of the diagnosis. In following up these cases it is interesting to note that a considerable proportion never developed the necessary symptom for such a diagnosis. A number have died of other diseases and only a comparatively small portion were cases of pellagra. A large part of these cases we now know suffered from tropical sprue, which was supposed not to occur in this country. Emphasis should be placed on the fact that in spite of an experience of several hundred cases of pellagra, extending over a period of ten years, any diagnosis made in the absence of skin lesions at that time was simply guesswork.

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[17] New York Med. Jour., December 18, 1909.

[18] Jour. Amer. Med. Assn. (Abs.), August 9, 1911.

[19] Tr. XVII Intern. Med. Cong., 1913, Sec. XXI, Trop. Med.

In an editorial in the *London Journal of Tropical Medicine and Hygiene*[20] the question of the probability of the identity of sprue and pellagra is strongly argued. The writer finds a marked similarity in the stools in both diseases as well as indicanuria and pathological changes in the intestinal tract which closely resemble one another. Tuczek found in pellagra an attenuation of the intestinal wall as a result of atrophy of the muscular coat and also occasional hyperemia and ulceration of the large intestine. The editorial notes, further, that in sprue the mucosa is almost entirely destroyed and is replaced by a structureless substance containing leukocytes. The submucosa appears much thickened and fibrous tissue is abundant. The muscular coat is greatly thinned. The argument is concluded by the statement that the gastro-intestinal symptoms which are prominent in both conditions are strikingly alike, and that results obtained from examination of the gastric contents, stools, blood, and urine reveal almost identical conditions. The writer thinks that the nervous and mental symptoms which occur in some cases of pellagra have been given undue prominence. Singer,[21] working with the Thompson-McFadden Pellagra Commission, found the incidence of pellagrous insanity to be 40 per cent., which is much lower than the incidence in my own cases in North Carolina. This observer regarded the nervous manifestations as toxic, subsiding with the disease activity. The definite cord degenerations, so well described by Tuczek[22] and so abundantly confirmed in this country in the few years in which such study has been possible, would throw the weight of evidence on the side of a disease to be ranked with syphilis, which it more closely resembles than any other. In one of our earlier cases there was definite degeneration of the columns of Goll and Burdach in the dorsal and lumbar cord. The patient was a negress, aged seventeen years, who was suffering the first outbreak. It is not reasonable to assume that reparation of this organic change would have occurred had she not succumbed. As a rule, organic nervous change does not occur until the victim of pellagra has suffered at least three outbreaks. When it does occur as a consequence of some toxic action it can be counted that the disease has reached the stage from which there is no recovery. While there is a toxic pellagrous psychosis unattended by any definite cerebral lesion, it is to be remembered that the spinal cord alone does not bear the brunt of the whole process. The growing tendency to make light of the nervous consequences of pellagra is to be deplored. Equally as much so as syphilis does pellagra attack the nervous system, and it might not be going too far to say, more so. It is probably in this one feature that we see the most distinctive difference between pellagra and sprue, for in the latter the nervous system does not suffer.

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[20] Jour. Trop. Med. Hyg., London, September 15, 1913.

[21] First Progress Report of the Thompson-McFadden Pellagra Commission.

[22] Klin. u. Anatom. Studien über die Pellagra, 1893.

In the beginning of the process it is often difficult to distinguish pellagra from sprue. Harris noted that in some of his cases the feces were typical of the sprue type, though the eruption of pellagra was present. It must be remembered in this connection that sprue may complicate pellagra. As a rule, the diarrhea of the two diseases may be readily distinguished. In pellagra the feces are generally more fluid, darker in color, not limited to the early hours of the day, and attended with more or less tenesmus and mucus. In sprue the stool is much larger than normal, quite light in color, acid in reaction, containing much gas, and usually occurring in the early hours of the day. The essential differences, however, are to be found in a chemical study of the feces. For this purpose we used the Schmidt test diet to determine the ratio between the fats and nitrogen intake and the output in the feces. In this work we were guided largely by the advice of Dr. J. H. Pratt.[23] We feel justified in the assertion that in pellagra the fat loss and the nitrogen loss in the feces are not abnormal. In one case of great gravity, which resulted in the death of the patient a few days after the observation, we found that the fat loss was 5 per cent. and the nitrogen loss 7 per cent. In another case of long standing the fat loss reached 17 per cent. and the nitrogen loss was 6.63 per cent. In sprue the findings are quite different. It will be recalled that Sir Lauder Brunton, Begg, Mayo Robson, and others found evidences of pancreatic inactivity or actual disease in spure. J. H. Pratt has called attention to the danger of error in counting a pancreas which is found on examination to be increased in hardness as a diseased organ. A number of these observers have noted the macroscopic findings of interstitial changes in the pancreas, but this alone should not constitute sufficient evidence of organic change. Oftentimes such an organ is capable of full function in spite of this apparent overgrowth of connective tissue. Begg thought that the failure of his yellowed santonin treatment in certain cases was due to complications, chief among which was pancreatitis. Cammidge found that in the urine and feces of fourteen cases pancreatitis occurred six times.

With all of this evidence pointing so strongly to a disturbance of the pancreas in sprue we carefully studied a number of cases of pellagra to determine this possible relationship. Our findings were entirely in accord with those of Myers and Fine[24] working with the Thompson-McFadden Pellagra Commission. They found that in pellagra there was practically normal utilization of the various foodstuffs. The fat utilization was good in all cases, though in three of their series of fifteen it was slightly below normal. At times we find the stools in pellagra to be acid. The Sahli glutoid capsule test in one case showed no return in the urine in five hours, and in this case there was an excess of meat fibers, but we found this to be exceptional. As a rule, the salicyluric acid appears in the urine in the normal time, the meat fibers are absent. The Schmidt beef-nucleus test, using the silk-gauze bags, was frequently tried, and in no case were there any nuclei to be found on sectioning and staining with eosin and hematoxylin. The test for trypsin showed its presence.

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[23] Amer. Jour. Med. Sci., March, 1912.

Observers in the tropics hitherto have been unable in many cases to distinguish between sprue and pellagra because of the absence of the skin lesions. The skin lesions of pellagra occupy only a small fractional part of the time of the outbreak, or may be so trivial as to be entirely overlooked. Such confusion may be avoided by a study of the feces. A fatty diarrhea alone would be the best single symptom for the diagnosis of sprue.

SUMMARY. 1. Tropical sprue occurs in the Southern States, where it is frequently confused with pellagra.

2. Spruce is a definite disease entity with a definite symptomatology, which when followed should cause no difficulty in diagnosis.

3. There is much evidence tending to justify a further study in order to determine whether the characteristic sprue stool is or is not due to a lesion of the pancreas. The deficiency of pancreatic function in sprue may be due to actual pancreatic change, or a disturbed intestinal function may play a part in the findings.

4. The only certain means of differentiation between pellagra and sprue is a study of the feces. Fatty stools with great fat and nitrogen loss are characteristic of sprue, while in pellagra the fat and nitrogen absorption are about normal even in spite of the diarrhea.

5. Sprue may complicate any of the intestinal diseases and add to the confusion in diagnosis, therefore, for the present at least, the diagnosis of pellagra should not be made in the absence of skin lesions except when the history of a former outbreak is definite.

I am especially indebted to Professor Isadore Dyer, of Tulane University School of Medicine, and to the librarian of that school for many kindnesses. To Mr. George F. Catlett I am indebted for material help in definitely determining the chemical differences in the stools of pellagra and sprue.

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[24] First Progress Report, Thompson-McFadden Pellagra Commission.

GANGRENE OF THE LUNG.

By George Douglas Head, B.S., M.D.,
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The diagnosis of gangrene of the lung is usually made without difficulty, provided the sputum and breath of the patient give out the characteristic, penetrating, fetid smell of decaying or burned flesh. In those cases where no such foul odor is present, and autopsy findings indicate that a considerable percentage of the cases fall into this group, the recognition of the nature of the pulmonary lesion is very difficult, and the diagnosis is usually made at autopsy.

In the following case the diagnosis of gangrene of the lung was made by plunging a long exploring needle into the area of lung involved and withdrawing about 5 c.c. of dark-colored fluid having the typical smell of gangrene and containing cellular elements of a peculiar type. Without this evidence the diagnosis of gangrene of the lung could not have been made, since neither the breath of the patient nor the sputum coughed up gave out an odor suggestive of gangrene.

This case also illustrates the value of this procedure in establishing the diagnosis of gangrene of the lung.

A case of typhoid fever complicated by thrombosis of the right femoral vein and gangrene of the base of the right lung terminating in death: Matt. H., aged thirty-three years, male, laborer, Bohemian, was admitted to the Minneapolis City Hospital December 12, 1905, complaining of cough and high fever. His family and personal history were both negative, except a five weeks' sickness three years before admission, the nature of which he was ignorant. He drinks and smokes moderately.

Patient's present illness dates back three weeks prior to his admission. He was working in the flour mills at the time. The patient was so ill and understood English so poorly that the details of his illness could not be secured. It was learned that he had had high fever, considerable cough, and some pain in his chest; that at times he had been delirious, and for the last week had been growing gradually worse.

The patient was a well-nourished, hardy looking laboring man; was nervous and restless; marked jactitation of arms and legs; pupils equal; foul breath; sordes on lips and teeth; heavily coated, dry tongue; semidelirious; respirations rapid and labored; some cough, with tenacious bloody sputum; pulse 110, temperature 104.

A careful physical examination was negative for organic disease outside of the lungs and the evidence of typhoid fever.

Posteriorly in the midscapular region upon the right side the percussion note was impaired at a point 3 cm. above the angle of the scapula, changing to a dull note from the angle of the scapula downward. The area of dulness was not movable. Vocal fremitus was not increased over this area of dulness. The breath sounds were suppressed in the area of dulness. A few fine moist rales could be heard on cough or forced breathing over this area. No tubular breathing could be heard.

The heart was negative; vessel walls somewhat thickened; abdomen moderately tympanitic; spleen not palpable. Leukocyte count 6200. Urine: no albumin, no sugar, no casts. Widal reaction positive. Sputum contained red blood cells and diplococci, but no tubercle bacilli.

The clinical diagnosis of typhoid fever was made, but the condition in the right chest was puzzling.

The patient remained in the hospital until his death—fourteen days. During this time he ran a high fever; ranging between 100.2° and 105°. Pulse 100 to 130. He was delirious much of the time, and extremely restless. His cough was persistent, at times paroxysmal and severe. The sputum was at times blood-tinged. At no time was there any odor to the sputum or the breath of the patient suggesting gangrene of the lung.

The bedside notes upon the lung condition at various dates during the illness were as follows:

Note of December 14: "Area of dulness in base of right lung is still present. Vocal fremitus is lost over this area. Bronchophony diminished. Many fine moist rales are interspersed with an occasional high-pitched sibilant rale heard in the area of dulness. These rales are most marked just below the angle of the scapula."

Note of December 15: "Area of dulness in right lung is unchanged. Vocal fremitus is absent over area of dulness. In this area on quiet breathing a friction-like, crackling sound can be heard close to the ear, most marked at the angle of the scapula. On deep inspiration and cough one hears over the area of dulness many coarse moist rales and an occasional sibilant rale. The upper part of the right lung and left lung exhibit no important physical signs."

The diagnostic comment upon the lung condition at this date reads as follows:

"The irregularity in the course of the temperature, the prolonged history of the illness, the absence of leukocytosis, and the absence of the usual physical signs of lobar pneumonia suggest strongly a tuberculous lesion in the base of the right lung. The sputum, however, is negative for tubercle bacilli. It is possible that we may be dealing with a massive pneumonia, or a lobar pneumonia complicated by a pleuritis with a thickened shaggy pleura, masking the distinctive signs of the lung consolidation. That the dulness is not due to an accumulation of fluid in the right pleural cavity is probable because of the presence of the pleural friction rub and the absence of movable dulness. There is no etiological factor to suggest infarct."

Note of December 16: "Sputum still bloody. Area of dulness in base of right lung as before. Absolute dulness begins about the angle of the scapula behind, at the posterior axillary line about the eighth interspace. Vocal fremitus is absent over dulness. Distant tubular breathing is suggested on auscultation. Many moist rales heard in base of left lung posteriorly; anteriorly over the fifth interspace a pronounced friction rub can be heard which is sharply localized between the parasternal and the left nipple lines."

Note of December 21: "When the patient lies on his left side the area of absolute dulness extends practically in a transverse line, around the right chest, beginning at the fifth interspace in front, in the sixth interspace in the postaxillary line, and at the angle of the scapula posteriorly.

Over area of dulness many loud moist rales can be heard with an occasional loud friction rub. Above the area of dulness even up to the apex of the lung, loud bubbling moist rales can be heard."

Today after the examination a long exploring needle of good caliber was introduced into the right chest just below the angle of the scapula posteriorly and over the area of dulness; 10 c.c. of a dark, chocolate-colored fluid were withdrawn (see Plate). The odor of this fluid was foul, and suggested at once gangrene of the lung. It contained (*a*) a few red cells, (*b*) a moderate number of leukocytes, (*c*) a moderate number of large mononuclear cells varying in size, the largest being about three to five times the size of leukocytes. In the protoplasm of these cells were many black pigment granules (Plate, *A*). Many black pigment granules were also seen free in the fluid and also in some of the leukocytes (Plate, *B* and *D*). These large mononuclear cells with pigment particles were alveolar epithelium undergoing degeneration. Some of these showed a thick cell membrane. The nucleus could not clearly be made out in many of them (Plate, *E*).

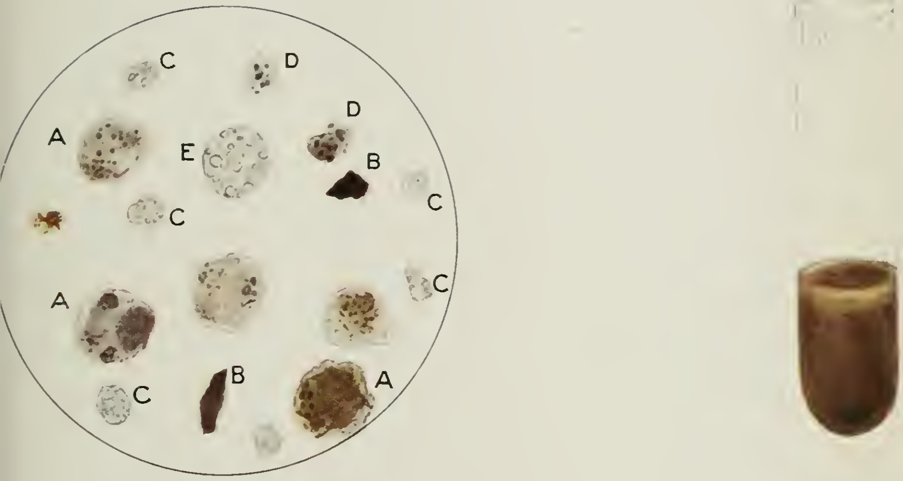
The diagnosis of gangrene of the lung was made upon the odor and character of the fluid withdrawn, and the patient was referred to the surgical side.

A lung drainage operation was done by Dr. J. C. Stewart. There was no fluid in the pleural cavity. The lower lobe of the right lung was gangrenous, soft, and friable. A foul-smelling, dark, grumous-looking fluid exuded when explored with the examining finger. Drainage from the gangrenous lung by tube was established.

The patient's condition remained unchanged after operation, except that the distressing spasmodic cough subsided and the temperature was not so high. The patient continued to lose strength, developed a talkative delirium, and died upon the fifteenth day after admission.

Postmortem diagnosis made twelve hours after death:

(*a*) Typhoid fever in fifth week with multiple ulcers in the ileum partially healed.



Puncture Fluid from Case of Gangrene of Lung.

A = Alveolar epithelium with blood pigment.
B = Free blood pigment.
C = Leukocytes.
D = Leukocytes with black pigment granules.
E = Alveolar epithelium undergoing fatty degeneration.

(*b*) Gangrene of lower lobe of right lung. Middle lobe of right lung collapsed.

(*c*) Embolism of branch of pulmonary artery with partially organized thrombus in vessel leading to gangrenous area. Ends of vessels in gangrenous lung area eroded.

(*d*) Thrombosis of right femoral vein, with organized thrombus of three or four weeks' standing.

(*e*) Adherent pleuritis of left pleura.

(*f*) Typhoid spleen.

THE LUETIN REACTION IN THE DIAGNOSIS OF TERTIARY AND LATENT SYPHILIS.

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The present report will concern itself largely with the aid which the luetin reaction offers in the diagnosis of tertiary and latent syphilis. The internist sees relatively little of primary and secondary syphilis, but he is constantly called upon to differentiate from other diseases the late manisfestations of syphilis of the various viscera. Syphilis of the heart and bloodvessels, of the larynx, of the lungs, mediastinal gummata, syphilis of the liver and spleen, syphilitic ulcerations of the mucous membranes, syphilis of the bones and joints, syphilis of the nervous system—these and many other of the internal manifestations of syphilis must often be weighed in differential diagnosis.

The renaissance in the study of syphilis which had its inception with Schaudinn's discovery of the Treponema pallidum, and which has received such tremendous impetus through the use of the Wassermann reaction and Ehrlich's salvarsan preparations, has not alone emphasized anew the astoundingly protein character of syphilitic manifestations, but has established new syndromes of syphilitic disease. As proof of this one has only to compare our present conceptions of cardiac and aortic syphilis with the teachings of less than a decade ago. Here, as in other fields, clinical pictures have been defined and clarified and certainty has replaced speculation.

Perfection of our diagnostic means, however, has not yet been attained. The Wassermann reaction has proved itself an invaluable and reliable adjunct to clinical observation, and when unequivocally positive, may be regarded as diagnostic of the presence of syphilis. Negative Wassermann reactions, on the other hand, are of limited value, for experience has shown that by no means every syphilitic patient gives a positive Wassermann reaction. This is especially true of the late visceral lesions, and fortunately it is in just this class of cases, who from their history and clinical condition incur the suspicion of syphilis and in whom the Wassermann reaction may be negative that the luetin test of Noguchi finds its most valuable application.

Luetin as prepared originally by Noguchi, and now manufactured by Parke, Davis & Co., and H. K. Mulford Company is a suspension of dead spirochetes obtained by emulsifying the medium in which the organisms have been cultivated with salt solution; the preparation is then heated in the usual way and preserved by the addition of 0.25 per cent. tricresol. As a test for syphilis, 0.04 c.c. of this preparation is injected intradermally (not hypodermically) with a fine hypodermic needle. A tuberculin syringe is very convenient for the injection.

It should be clearly understood that the luetin and Wassermann reactions do not depend upon the same biological conditions of the body for their production. The exact mechanism of the Wassermann reaction is unknown, but it is certainly dependent upon some definite alteration of the blood serum whereby a certain nonspecific antigen is fixed in some way to complement. The luetin reaction, on the contrary, is a test of specific cutaneous hypersensitiveness or allergy, and would seem to be a cellular reaction. Luetin is exactly analogous to tuberculin in its cutaneous action, and is one of a constantly increasing group of preparations devised for the detection of specific cutaneous hypersensitiveness due to general infection. Mallein, typhoidin, and streptothricin are other examples. A discussion of this interesting group of reactions will be found in the recent article by Gay,[1] and need not detain us at this time.

If one bears in mind, then, that the luetin and Wassermann reactions, though often mutually corroborative, are never competitive, and that the finding of a positive luetin and a negative Wassermann reaction in the same patient involves no essential incongruity, it will simplify the problem of adjudging the value of luetin as a test for syphilis.

Noguchi and others to whom he has sent his preparation have studied the luetin reaction in the various stages of syphilis for the past three years, and during this time a considerable volume of evidence has accumulated. Noguchi[2] has recently summed up this evidence as follows: "In primary syphilis the luetin reaction is positive in less than 30 per cent. of cases and the reaction is mild in type. In secondary syphilis about 40 per cent. of 630 cases gave positive reactions, and here too the reactions were not pronounced. In congenital syphilis about 70 per cent. of cases reacted positively. In tabes and general paresis 60 per cent. gave positive reactions, whereas in tertiary syphilis 90 per cent. gave positive luetin tests and the reactions were very intense."

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[1] Amer. Jour. Med. Sci., 1915, cxlix, 157.

[2] New York Med. Jour., 1914, p. 319.

It will thus be seen that as a test for syphilis in the primary and secondary stages the luetin test is inferior to the Wassermann reaction; in tertiary and latent syphilis, however, the luetin test has proved very reliable, and, indeed, it is in just this class of cases, which constitute by far the larger part of the syphilitic patients who present themselves to the internist for diagnosis, and in which the Wassermann reaction is not infrequently negative, that the luetin test finds its most useful application. I shall illustrate this point later with several instructive cases.

The technique of the luetin test is simple, but its correct interpretation requires some experience with the reaction. With the luetin kindly furnished me by Dr. Noguchi, 0.04 c.c. diluted with an equal quantity of salt solution was injected intradermally, care being exercised to make the injection into and not beneath the skin. The reaction will not occur typically if the material is injected hypodermically. Most of my experience has been with the original luetin of Noguchi, but recently several manufacturers have furnished me with their products, and I have carried out a series of parallel tests, using the well-proved luetin of Noguchi as a control. Briefly, one may say that the luetin of the manufacturers seems reliable (Figs. 3, 5 and 6). The size of the dose of luetin employed is of importance, for if too much is used non-specific inflammation is produced, which though never typical of the luetin reaction, may yet prove confusing. Several instances of this have come to my notice recently, and observation of these cases at intervals over a ten-day period convinced me of the non-specific character of the reactions, a conclusion which was supported by the negative luetin tests subsequently performed.

The luetin reaction varies somewhat in character in various patients, though always, in my experience, exhibiting constant characteristics in the same patient when several tests are performed. I have performed three tests at intervals of one month or more in several patients and the reactions have always been identical in type. This is a point of some importance in judging the specificity of the luetin test.

The reaction usually develops promptly in twenty-four to forty-eight hours, though it may be delayed or latent in type, developing ten days or two weeks after the injection. I have in one instance seen a typical reaction develop twenty-one days after the injection, the arm in the meantime having an absolutely normal appearance and showing no trace of the injection. This curious and interesting phenomenon should always be borne in mind when pronouncing upon the negative or positive character of a test. When negative the injection site shows as a maximum reaction a nodule the size of a match-head or smaller. This subsides promptly and never pustulates.

The positive reaction begins by the development of an intensely congested and reddened nodule, varying roughly from a green pea to a cherry in size (Fig. 1). This nodule is surrounded by an area of inflammation which seldom exceeds 1 cm. in diameter, though occasionally larger. The inflammatory nodule is scarcely painful at all, constrasting strongly in this respect with pyogenic inflammations. In an experience of more than 200 injections I have had no patient complain of the reaction causing more than negligible pain, and one is frequently surprised at the apparent absence of pain when the nodule is palpated. This inflammatory nodule may represent the entire reaction, persisting for a week and slowly subsiding; but this is rarely true, the great majority of the reactions progressing through two characteristics later stages. The centre of the nodule softens after a few days (Fig. 2), ruptures (Fig. 3) and discharges a few drops of thick, purulent material which under the microscope shows no bacteria. A scab now forms and the pustule undergoes a retrogression. As it diminishes in size the skin over the entire inflamed area alowly desquamates (Figs. 4 and 5). These various stages of the reaction are repeated with great regularity, and give to the test a very characteristic picture. The reaction gradually subsides in from ten days to three weeks, leaving a slight pigmentation, but, as a rule, no permanent scarring.

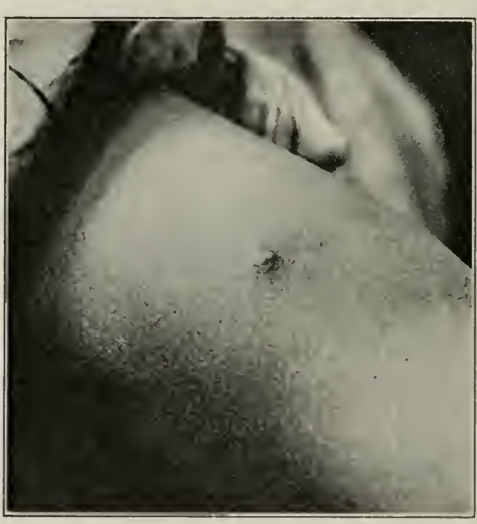

FIG. 1.—Twenty-four hour luetin reaction.

Having thus briefly defined the limitations of the luetin test and described the characteristics of the reactions, we may proceed to a consideration of certain illustrative clinical cases. The luetin test, like the Wassermann reaction, has but slight negative value. When positive, however, it is in my experience diagnostic of syphilis.

The most suitable cases for accurately testing the reliability of luetin are those presenting external evidence of tertiary syphilis in the form of gummata or gummatous ulcerations. Of such cases I have tested fourteen with luetin, and in every instance the reaction was frankly positive, and all gave positive Wassermann reactions.

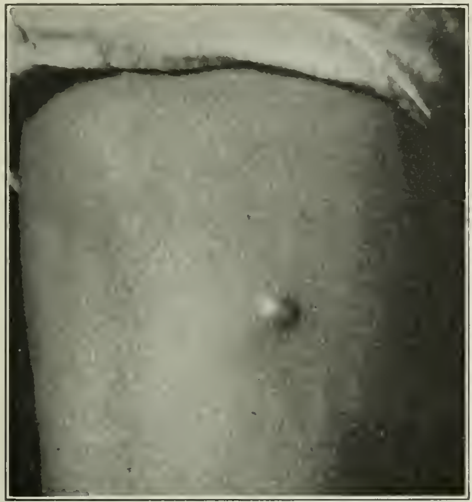

Fig. 2.—Reaction at end of three days. The nodule has softened and is on the point of discharging.

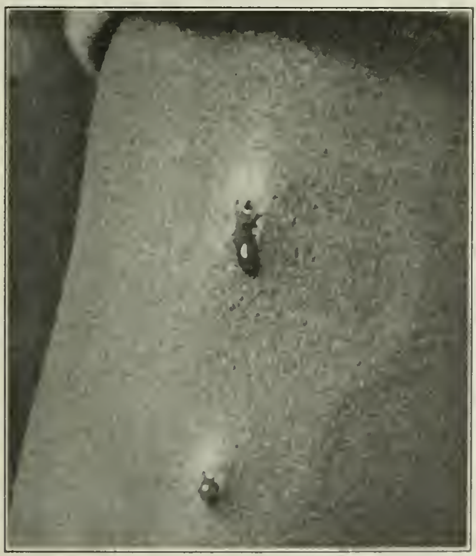

Fig. 3.—Pustule stage of the luetin reaction. (Noguchi luetin above.)

One very instructive case is worthy of note. The patient was a colored man aged twenty-three years, who presented himself with a large ulcerated area over the manubrium. He had been under treatment for this ulcer in a hospital, mercury inunctions being given for the supposedly syphilitic lesion. A Wassermann test was done and was negative, but because of the previous mercury

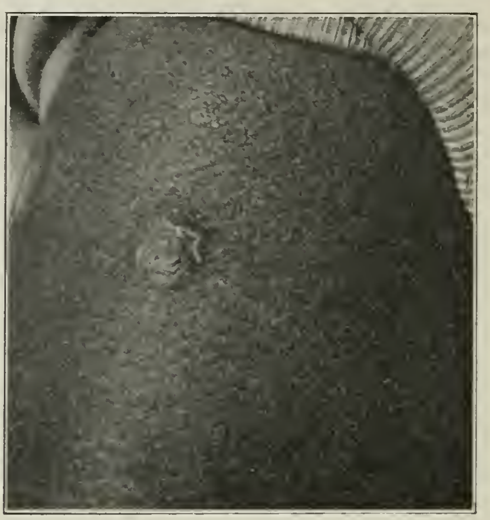

Fig. 4.—Final stage of the reaction. The nodule has pustulated, a scab has formed, and the area of inflammation is desquamating.

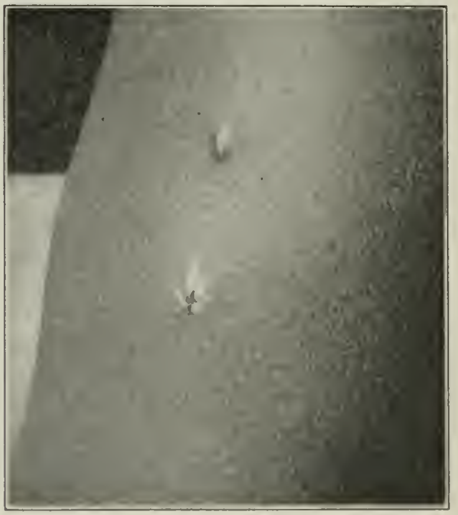

Fig. 5.—Twenty-four hour luetin reactions. (Noguchi luetin above.)

treatment this could not be accepted as final. Two luetin tests were performed, the second four weeks after the first, and both were negative. These tests threw considerable doubt upon the correctness of the original diagnosis of the syphilitic ulcer, but mercury inunctions with potassium iodide were given and the ulcer was dressed with ungent. hydrarg. After one month of this vigorous treatment the ulceration showed very little indication of healing, and it was felt that since the therapeutic test confirmed the results of the Wassermann and luetin tests the original clinical diagnosis was incorrect.

For the internist the most important group of syphilitic cases are those presenting clinical evidence of visceral syphilis. My own experience with the luetin test has been largely confined to medical cases presenting themselves for diagnosis with symptoms which suggested visceral syphilitic lesions. Much of the present work has been done upon negro patients who from the tremendous prevalence of syphilis among them offer a most favorable material for such a study. One is impressed with the frequency of severe heart and vascular lesions in negro patients under forty-five years of age. The lesions are almost uniformly situated at the aortic valve, and in addition there are usually symptoms and signs of aortic disease. On purely clinical grounds aortic valve disease and aortitis with dilitation, occurring in young or middle-aged people, have long been regarded as almost certain evidence of syphilis. There are, of course, exceptions to this, as in the case of certain forms of pyogenic malignant endocarditis due to Pneumococcus or Streptococcus pyogenes and viridans, but these cases rarely survive, and therefore seldom enter into the differential diagnosis of chronic aortic valve disease in the middle aged.

Twelve cases in which the history, symptoms, and physical findings justified the diagnosis of cardiac and vascular syphilis have been studied with the aid of the Wassermann and luetin tests. These cases were seen from seven to twenty-five years after their probable infection and thus fall into the group of tertiary visceral syphilis. Of these twelve cases all gave positive luetin reactions, whereas only seven yielded positive Wassermanns. Several of these cases will be detailed, for the subject of cardiac and vascular syphilis is one of great importance, as has been recently emphasized anew by the excellent studies of Brooks.[3]

Recently a colleague of mine stated that he had under his care a man, aged twenty-six years, with severe double aortic valve disease with retromanubrial dulness and slight tracheal tug, in whom the Wassermann reaction was negative. He had been unable to elicit any history of tonsillitis, acute rheumatism, or chorea, and there was no history of acute endocarditis. He felt that the case was syphilitic despite the negative Wassermann, and referred him to me for a luetin test, which was frankly positive.

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[3] Amer. Jour. Med. Sci., 1913, cxlvii.

A second case illustrating the point just made is as follows: J. H., a colored man, aged thirty-two years, came complaining of pain in the chest under the sternum, which became worse at night, nervousness, and pain in the lumbosacral region. He admitted having had syphilis ten years ago, and treatment was taken for two months. On physical examination there was general glanular enlargement of moderate degree, both epitrochlears being enlarged, the heart was slightly enlarged, the relative cardiac dulness reaching 1 cm. beyond the nipple line, and there was definite retromanubrial impairment. No pulsation was visible in the aortic area. There was a diastolic aortic murmur and the second aortic sound was accentuated. A slight tracheal tug could be felt. The pain in the lumbosacral region was quite severe, but no local cause for this could be demonstrated. This is a condition which I have seen frequently in syphilitics, and it is relieved so promptly by vigorous antisyphilitic treatment that it would seem to be of luetic origin. The Wassermann reaction was negative. A luetin test was done on December 5 and December 18. The reaction was strongly positive, as evidenced by an intensely inflamed nodule, the size of a cherry, which pustulated on the fifth day. The reaction slowly subsided, but a slight nodule was palpable after one month.

A third and final case from this group will illustrate the value of the luetin reaction in differentiating aortic and vascular disease due to syphilis from atherosclerosis of the usual type.

J. S., aged forty-eight years, came complaining of headaches, "pains around the heart," and nocturnal frequency of urination. Of importance in his past history was an attack of what seems to have been syphilis at the age of twenty-four years. He was under treatment for eight months, and says he has never had any trouble since.

Briefly, his physical examination revealed a thin, poorly nourished man with thickened peripheral arteries and a blood-pressure of 180. No glandular enlargement. The heart was enlarged 1.5 cm. to the left of nipple line, and the second aortic sound was loud and ringing. There was marked retromanubrial dulness and faint, visible pulsation in the second right interspace, together with a moderate tracheal tug. The urine showed a distinct cloud of albumin with a few hyaline casts. Physical examination was otherwise negative. The Wassermann was negative, but two successive luetin tests were strongly positive (Fig. 6).

It would thus seem that the luetin reaction in cardiovascular syphilis is very reliable, and that certain cases will give both Wassermann and luetin reactions, while others show a negative Wassermann and positive luetin. Since the Wassermann and luetin reactions do not depend upon the same biological conditions for their productions, it is not strange that they sometimes show results which do not agree. The work of Vedder and Borden,[4] who examined 744 inmates of the Soldiers' Home in Washington, using the Wassermann and luetin reactions, is very valuable, for, as they state, 80 per cent. of the inmates of the Home are over fifty years of age, and hence when syphilitic they almost certainly suffer from tertiary manifestations or the disease is latent. In this class of cases they found 20 per cent. positive Wassermanns in 744 individuals and 32 per cent. positive luetin reactions. Obviously, then, 12 per cent. of their cases gave negative Wassermanns and positive luetins. They concluded that "the luetin test is therefore more delicate than the Wassermann as a routine test in the class of cases we examined, that is, tertiary and latent syphilis."

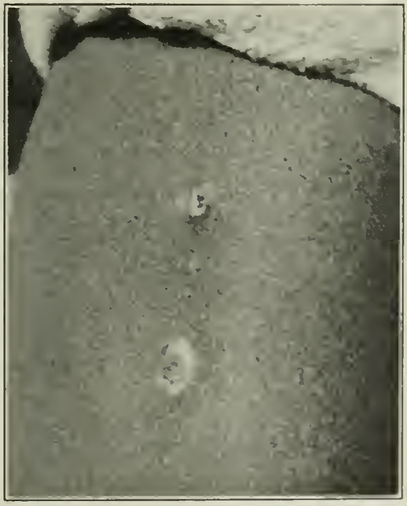

FIG. 6.—Comparative luetin reactions at four days. (Noguchi luetin above.)

It is well to emphasize strongly, however, that the luetin test does not seem destined to supplant in any way the Wassermann reaction. In late stages of syphilis luetin is a most valuable adjunct and will unquestionably demonstrate the presence of syphilis in certain cases which do not give a positive Wassermann reaction. The Wassermann reaction is applicable to all stages of syphilis beyond the primary, whereas the luetin test should be reserved for the detection of latent syphilis and the various manifestations of tertiary syphilis. The test must be used with discretion and with a proper consideration of the history and physical findings. In properly selected cases it furnishes information of the greatest value and the ease and inexpensiveness of its application strongly recommend it. Furthermore, many patients are aware of the significance of blood tests, and some resent the implication. This is a minor consideration, but the objection does not apply as yet to "skin tests."

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[4] Jour. Am. Med. Assn., 1914, lxiii, 1750.

The latent or delayed type of luetin reaction is of peculiar interest and importance. In my series it has occurred in about 3 per cent. of cases. Following the injection the skin shows no evidence of specific reaction whatsoever. After a period varying from one to three weeks a typical luetin nodule develops which passes through the stages of pustulation and desquamation described. These delayed reactions furnish the strongest proof of the specificity of the luetin tests. One of my patients, a white male, aged forty-five years, with a history of syphilis contracted seventeen years ago, showed a delay of ten days in the appearance of the reaction. After three weeks he was given a second luetin test, the Wassermann reaction having been reported as negative in the meantime. Again there was a delay of nine days before the typical nodule developed. Several cases of my series have shown delays of from ten to fourteen days in the development of the reaction, and in one case the delay was twenty-one days. The character of the inflammatory reaction when delayed does not differ at all from the usual prompt response; the nodule pustulates, a scab forms, and desquamation ensues.

From the study of the luetin reaction in two hundred medical cases presenting themselves for diagnosis the following conclusions are drawn:

1. The luetin reaction when positive is absolutely specific. I have not seen a single positive reaction in a case free from symptoms and physical signs of syphilis.
2. The reaction is of very limited value in other than tertiary cases.
3. The luetin reaction is a more delicate test for latent and tertiary syphilis than is the Wassermann reaction.
4. Patients suffering with visceral syphilis give positive luetin reactions with great constancy. This seems especially true of cardiovascular syphilis.
5. The luetin test represents a distinct advance in the diagnosis of syphilis, and is a very helpful supplement to the Wassermann test in the diagnosis of tertiary syphilitic lesions.

To Dr. E. Guy Hopkins, associate professor of pathology, Medical College of Virginia, who performed the Wassermann tests upon the cases reported in this paper, I am greatly indebted. My thanks are likewise due to Dr. Hideyo Noguchi, of the Rockefeller Institute, who supplied me with abundant luetin for this study.

FRIEDLÄNDER BACILLUS PNEUMONIA: WITH REPORT OF CASES.

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Introduction. Since the Bacillus mucosus capsulatus was identified by Friedländer,[1] in 1882, its significance in infectious diseases, notably pneumonia, has not been well defined. The objects of this paper are to present additional evidence concerning the relationship between the Bacillus mucosus capsulatus and certain cases of acute lobar pneumonia, and to call attention to a form of pulmonary disease which is discussed inadequately in modern text-books and unrecognized often during life.

Two quite contradictory views have been held. On the one hand Fraenkel,[2] confirming Sternberg's[3] observations, was the first to demonstrate that the Pneumococcus lancelatus was the usual bacteriological factor in produing pneumonia. He believed, however, that the Bacillus mucosus capsulatus was undoubtedly associated with certain types of this disease as a secondary invader. Curry,[4] working more recently on the subject, concurred essentially with this opinion. Weichselbaum,[5] on the other hand, while recognizing that the pneumococcus was the chief etiological agent in pneumonia, believed that about 5.5 per cent. of all cases of "croupous" pneumonia were caused solely by the Bacillus mucosus capsulatus. Honl[6] believed the percentage to be somewhat higher (8 to 10 per cent.). Marchand and his pupils also entertained the opinion of Weichselbaum, and were the first to give definite pathological facts in its support. The same contradictory statements are still found in medical text-books. Osler,[7] speaking of the Bacillus mucosus capsulatus as an etiological agent in pneumonia, says "it may cause bronchopneumonia and other infections, and is not a cause of genuine lobar pneumonia." Allbutt[8] states that the "pneumobacillus" is found in the lung tissue, producing an acute inflammation, but of the bronchopneumonic type, rather than the lobar. Osler and McCrae in their recent *System of Medicine* (1914) make no reference to the possible relation between pneumonia and the Bacillus mucosus capsulatus. Strümpell,[9] Krehl,[10] and Lord,[11] on the other hand, are of the opinion that this organism may cause a definite form of lobar pneumonia. Thus it is seen from the review of the literature that the prevailing opinion is that a lobar pneumonia of the so-called Friedländer type exists.

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[1] Virchows Arch. f. path. Anat., 1882, lxxxvii, 319; Fortschr. d. Med., 1883, i, 715.

[2] Ztschr. f. klin. Med., 1886, ii, 437.

[3] Trans. Path. Soc. of Phila., 1883–1885, p. 182.

[4] Jour. Exper. Med., 1899, iv, 169.

[5] Med. Jahrb., 1886, 483.

[6] Lubarsch and Ostertag, Allg. Path., 1896, i, 677.

[7] Principles and Practice of Med., 1912, 8th ed., 77.

[8] System of Med., 1909, v, 196.

Experimental Work. The experimental work on the subject of "Friedländer" pneumonia is surprisingly meager. The work of Kokawa[12] is altogether too incomplete to base any conclusions upon. This author experimented on eight guinea-pigs and seven rabbits, and in two instances, after the injection of a bouillon culture of the Bacillus mucosus capsulatus directly into the lung, thus introducing the element of trauma, found lesions resembling those seen in man. In one of these cases the exudate from the lung showed the presence of cocci associated with the Bacillus mucosus capsulatus. In one instance an intratracheal injection gave small microscopic foci of bronchopneumonia. Other experiments made in the same way gave negative results. Lamar and Meltzer[13] more recently have reproduced the disease successfully in two dogs after intrabronchial insufflation of a culture of the Bacillus mucosus capsulatus.

Previous Clinical and Pathological Observations. A considerable number of cases of so-called "Friedländer's" pneumonia have been reported thus far in the literature. Relatively few of these, however, can be utilized to establish the relationship between pneumonia and the Bacillus mucosus capsulatus. A large number of cases have no accompanying protocols and the diagnosis is often based on inadequate clinical and pathological findings. Cultural findings from the blood, sputum, or lung exudate are by no means sufficient evidence to establish the etiology of pneumonia. This has been pointed out by Weichselbaum, Smith, and others. Coverglass preparations from the lung exudate, cultures from the blood, antemortem and postmortem, cultures from lung puncture, and sections from the lungs stained by Gram's method, offer more reliable evidence for the correct diagnosis. Even these methods may not determine conclusively the organism that is the original cause of the condition. The rapid growth of the Bacillus mucosus capsulatus may obscure the presence of cocci in a short time. This is especially true in tissues. A large number of cases have been reported in which other organisms than the Bacillus mucosus capsulatus have been found. Many authors have thus been led to believe that in these cases the Bacillus mucosus capsulatus exists as a secondary invader in connection with pneumonia. It is evident that the so-called "mixed" cases of pneumonia cannot be utilized in this paper. It is of interest in this connection that the Bacillus mucosus capsulatus has been found apparently as the sole etiological factor in many infections other than pneumonia, *i. e.*, pleurisy, pericarditis, meningitis, general septicemia. In this respect it is quite comparable to the pneumococcus. Thus far only about thirty-three cases of pneumonia have been reported so fully that they can reasonably be considered to have been produced solely by the Bacillus mucosus capsulatus. Some of these may be questioned as unequivocal cases of so-called "Friedländer" pneumonia. Brief reference will be made to the most important of the most authenticated cases. Comba,[14] in 1896, reported a case in a child of six days. The autopsy showed bronchopneumonia. A pure culture of the Bacillus mucosus capsulatus was obtained from the heart's blood, and from the lung exudate, one hour postmortem. Thiroloix[15] found the organism in pure culture from the lung exudate of a man, aged fifty-six years. The duration of the disease in this case was six days. Smith[16] reports the case of a man, aged forty-nine years, who died of pneumonia complicated by organic cardiac disease. The duration of the pneumonia was not given. Cultures and sections of the lung showed the organism in pure culture. Howard[17] and Beco[18] each found the organism in pure culture at autopsy. Brinckerhoff and Thompson[19] record a thoroughly studied case from which a pure culture of the organism was found in the heart's blood at autopsy. The diagnosis was based also on cultural findings from the lungs, cover-slip preparations stained by Welch's and Gram's methods, sections of lung stained by Gram-Weigert method, with methylene blue, and upon inoculation of animals. This patient was fifty-three years of age, and died about five days after the onset of his symptoms. Philippi[20] and Lenhartz[21] each reports a case in which a pure culture of the organism was found during life. Kokawa[22] (working in Marchand's laboratory) added nine cases in which the diagnosis was based on pathological findings. He was the first to make a careful study of the condition from a pathological point of view. Stühlern[23] reports ten cases. Only three of these can be regarded as being due to the Friedländer bacillus. Although three of the ten are said to have survived, it is impossible to state whether other organisms than the Bacillus mucosus capsulatus were associated with the disease. Etienne[24] records two cases in which the Bacillus mucosus capsulatus was recovered in pure culture from various organs at autopsy. Apelt[25] adds seven cases which may reasonably be considered as genuine cases of Friedländer pneumonia; all of these died. The average age was about fifty. In one patient, aged forty-six years, the organism was recovered from the blood on the second day of the disease. Another case, aged thirty years, gave a sterile blood culture on the fourth day. A resection of the ribs was done, a cavity found, and much pus recovered, which showed a pure culture of Bacillus mucosus capsulatus. The man died on the twenty-eighth day of the disease. Another of Apelt's cases also showed a large cavity in the lung at autopsy. Of special interest is a case that died on the second day of the disease. The autopsy showed complete consolidation of the right superior lobe with foci in the right inferior lobe. Mosny and Pruvost,[26] Brissaud,[27] Gouget and Moreau,[28] Moisejew,[29] and Weill[30] all have reported cases in which the Bacillus mucosus capsulatus was found in the blood in pure culture, sometimes both antemortem and postmortem. All of these cases died.

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[9] Spez. Path. u. Therap., 1914, Bd. i, 262.
[10] v. Mering's Lehrbuch d. Inneren Med., 1911, p. 233.
[11] Diseases of Bronchi, Lungs, and Pleura, 1915, p. 234.
[12] Ztschr. f. Hyg. u. Infectionskrankh., 1905, l, 364.
[13] Jour. Exper. Med., 1912, xv, 133.

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[14] Jahresb. u. d. Fortschr. d. path. Microorg., 1896, xii, 101.

[15] Bull. et mém. Soc. anat. de Paris, 1897, xi, 152.

[16] Jour. Boston Soc. Med. Sci., 1897–1898, ii, 174.

[17] Philadelphia Med. Jour., 1898, i, 336.

[18] Rev. de Méd., 1899, xix, 461.

[19] Reports Boston City Hosp., 1901, p. 149.

[20] München. med. Wchnschr., 1902, xlix, 1884.

[21] Die sept. Erkrankungen. Nothnagel's spez. Path. u. Therapie, III, II.

[22] Deutsch. Arch. f. klin. Med., 1904, lxxx, 39.

[23] Centralbl. f. Bakteriol., 1904, xxxvi, 493.

During the last year, in a relatively small series of cases of pneumonia at the Peter Bent Brigham Hospital, four pulmonary infections associated with the Bacillus mucosus capsulatus have been studied. These cases illustrate well the clinical and pathological findings associated with this form of infection. One case (Case I) in particular adds further evidence concerning the existence of a certain type of pneumonia caused by an encapsulated bacillus because of the short duration, the typical symptoms and physical signs of pneumonia in a patient in whom during life and at autopsy the Friedländer bacillus was found in pure culture.

Case I (Med. No. 1125).—The history is that of a charwoman, aged sixty-five years, whose family history is unimportant. She had erysipelas at forty, pneumonia at fifty-four. She had had symptoms of cardiac insufficiency during the past year and was treated at this hospital. Patient's duties were such that she was obliged to rise at 4.30 A.M., working until 10.00 A.M. On the day of admission she rose as usual, but while going to work became thoroughly chilled. This did not prevent her from performing her morning's duties. She returned home at 10.00 A.M., complaining of feeling cold and weak. About this time she began to cough

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[24] Arch. de méd. expér. et de anat. Path., 1895, vii, 124.

[25] München. med. Wchnschr., 1908, lv, 833.

[26] Bull. et mém. Soc. Méd. d. hôp. de Paris, 1913, p. 395.

[27] Lyon méd., 1912, lxxx, 205.

[28] Bull. et mém. Soc. méd. d. hop. de Paris, 1912, xxxiv, 296.

[29] Bolnitschanja Gazetta Botkina., 1900, xx and xxii (quoted from Apelt, 25).

[30] Lyon méd., 1914, xiii, 13; cxxii, 133.

(no mention is made of any expectoration). She cooked her dinner and ate heartily, planning to return to work in the afternoon. About this time she had another chill, and began to expectorate blood-tinged sputum. A physician was called immediately, and she was advised to go to the hospital. No pulmonary signs were made out at this time. At 5.00 P.M. of the same day, two hours after being seen by her local physician, she entered the hospital. Her respirations were shallow, fifty per minute; she complained of severe pain in the right side of her chest. There were signs of consolidation at the right apex, and coarse rales, were heard over both chests. The pulse was accelerated (100 per minute), blood-pressure 100 systolic, temperature 101.8° F., white count 26,000. At entrance to the hospital the sputum was blood tinged, copious, distinctly slimy, and showed organisms in pure culture corresponding to the Bacillus mucosus capsulatus. A blood culture taken at entrance also showed a pure culture of this organism. The subjective and objective symptoms became progressively worse, cyanosis was extreme, patient became comatose and pulseless during the night, her temperature reaching 105° F. by rectum. The blood-pressure fell to 60 mm. (systolic), the white count to 3800. Death occurred at 1.38 P.M. the following day—thirty-one and a half hours after the initial chill, and in less than twenty-four hours from the time the patient went to bed. A specimen of sputum was injected intraperitoneally into a mouse. The organism in the mouse's peritoneal exudate showed no agglutination with sera from various strains of pneumococci.

Autopsy. The autopsy was performed one hour after death. The pathological findings of special interest centred about the lungs. These were voluminous and completely filled the pleural cavities. The pleura on the left was everywhere smooth and glistening. There were a few firm fibrous adhesions over the right apex, also many fibrinous adhesions over the anterior and lateral surfaces of the pleura approximating the upper and middle lobes of the right lung.

The left lung weighed 415 grams, the right 965 grams. The surface of the left lung was smooth and glistening, and had a mottled effect, due to brilliant red areas outlined by pigmented striations between the lobules. There was a small region just at the base of the upper lobe which was firmer and more leathery than elsewhere. It was non-crepitant, and on cross-section dark red and very moist. The tissue floated in water. Cross-section of the upper lobe at other levels showed normal findings. There were a number of elevations over the surface of the lower lobe. These represented very definite, discrete, firm, consolidated nodules, 2 to 3 cm. in diameter, within the lung parenchyma. A slight opacity over the visceral pleura demarcated the nodules. On cross-section the cut surface was fairly homogeneous, very moist, and a sanguineous, slightly tenacious, slimy, mucoid material exuded on pressure. The color varied from a brownish red in some areas of consolidation to gray. There was also variations in the character of the exudate. Over the grayer nodules it was more tenacious; here also the parenchyma could be scraped off more easily.

The surface of the right lung was somewhat irregular, due to nodular elevations of varying heights. The pleura over these areas was cloudy. A thin greenish exudate was seen in places. The apex was crepitant. The remaining portions of this lobe, as well as the middle lobe, were completely consolidated. On cross-section of the crepitant apex nothing remarkable was noted. The cut surface of the consolidated portion gave a very striking picture. A tenacious, slimy, soapy, gray, slightly sanguineous exudate was seen. After this had been removed the surface had a mottled effect and suggested strongly the coalescing of smaller discrete nodules. The parenchyma could not be scraped off with ease with a knife; the alveoli could not be made out. A few small granular masses were noted. In the middle and lower lobes focal areas of consolidation, 2 to 4 cm. in diameter, were found; these showed characteristics similar to those described in the left lower lobe. In all about two-fifths of the lung parenchyma was consolidated.

Cultures taken from heart's blood, lungs, liver, and spleen, on plain agar and plain bouillon, all showed in twenty hours a pure growth of the Bacillus mucosus capsulatus. Smears from the lung exudate stained by Welch's method for demonstrating capsules showed enormous numbers of capsulated bacilli. Smears stained by Gram's method showed numerous Gram-negative bacilli, varying greatly in length. The organisms were both extracellular and intracellular.

Microscopic Findings. Sections were fixed in Zenker's fluid and in formalin stained with hematoxylin and eosin, methylene blue and eosin, and by Gram's method. The sections from the focal areas presented a rather non-uniform appearance. Certain fields showed alveolar spaces dilated and completely filled with bacilli and a few scattered pus cells. The organisms were both intracellular and extracellular. The alveolar exudate varied greatly, especially in regard to the number of organisms present. The spaces containing few organisms were completely filled with polymorphonuclear and red blood cells occurring in about equal numbers. The demarcation between the alveoli containing and those not containing bacilli was often sharp. Oftentimes the demarcation was indicated by fibrous bands separating lobules. Sections taken from larger areas of consolidation showed similar characteristics. Here the alveolar septa were often ruptured and indistinguishable. The exudate contained many desquamated vacuolated cells which were relatively uncommon in the focal areas. These cells often contained 10 to 15 capsulated bacilli. Capsulated forms were also within the polymorphonuclear cells. The cells of the exudate of the large consolidated areas showed poorer staining qualities than those in the focal areas. The capillaries were everywhere distended with erythrocytes, and oftentimes there were localized foci of hemorrhage. Few bronchi were encountered in the sections studied. These showed practically the same variations in the character of the exudate as did the alveoli. The mucosa of the bronchi was everywhere intact. The lighter areas noted in gross corresponded to the alveoli completely filled with organisms, while the hemorrhagic interstitial tissue represented spaces filled with polymorphonuclear and red blood cells.

Case II (Med. No. 1265). — The patient was a woman aged sixty-five years. Her past history and habits were unimportant, except that she had had repeated attacks of cardiac insufficiency. Four days before admission to the hospital, following a rather strenuous day of shopping, she became very weak and complained of pain in the left chest. She developed a cough, and expectorated profuse amounts of blood-tinged sputum.

On physical examination the signs of extreme prostration were marked. There were signs of consolidation over the left upper lobe. There was a systolic murmur, loudest over the second interspace to the right of the sternum. Two days after admission patient became comatose. There was marked dyspnea, the pulse became feeble and more accelerated, and she died suddenly on the third day (that is, approximately seven and a half days after onset). The temperature reached a maximum of 102.5°; the white count was 13,000. The sputum was rusty, very tenacious, and contained abundant "cocci." (It is of interest to note the absence of the recognition of capsulated organisms in view of the pathological findings.)

Autopsy, A–14–38. The autopsy was performed twenty hours postmortem. The pathological findings of interest centred about the lungs.

The left pleural cavity contained about 200 c.c. of yellow turbid fluid. The parietal pleura was smooth and glistening. The visceral pleura of the superior lobe, anteriorly and posteriorly, was covered with a thin, fibrinous, slightly yellow exudate. Cloudy, grayish opacities were noted over the anterior surface of the inferior left lobe. The left lung weighed 1075 grams, the right 390 grams. The superior lobe of the left lung was markedly enlarged and completely consolidated except for creptitant margins. The aortic arch marking was clearly shown. Pale, grayish-white, raised nodules gave the surface, especially along the pericardial portion, a roughened appearance. These nodules were demarcated by lymphatic margins, and suggested a lobular distribution of the process. Section through the middle of the lobe showed a moderately homogeneous appearance except for a mottled effect in peripheral areas, due apparently to the lobular distribution, and suggesting incompleteness of the consolidation. The color was a light gray. The tissue at the apex between the gray consolidated areas suggested interstitial edema. A narrow zone along the inferior portion of this lobe was clearly demarcated from the overlying gray consolidated portion by its brilliant red color, crepitancy, and the clear outlines of the alveolar structures. The cut surface of the massive consolidated area was covered by a mucoid, viscid material. This exuded on pressure from a great many points. The scraped surface was slightly granular. The tissue was extraordinarily friable. In places it had softened, leaving a cavity without definite walls. In other places the tissue broke down on touching. The cut surface in certain areas of the consolidation, although soft, was pale red, in other areas in its opacity it resembled a completely infarcted zone. The opaque area often projected sharply into the surrounding tissue. Although practically the entire lung was consolidated, the consolidation in various places differed apparently in point of age.

The inferior lobe of this lung, also the middle and inferior lobes of the right lung, showed a few isolated non-crepitant nodular areas. On cross-section these were somewhat raised and bright red in color, and suggested areas of bronchopneumonia. In other respects the findings were not unusual.

Microscopic Findings: Sections were fixed in both formalin and Zenker's fluid, and stained with Gram's method, methylene blue and eosin, and hematoxylin and eosin. Those taken from various portions of the consolidated portions of the left lung all showed essentially similar findings. The alveolar spaces were uniformly filled with an exudate consisting chiefly of polymorphonuclear and vacuolated epithelial cells. The large vacuolated cells often contained capsulated bacilli. This type of cell was often very numerous, and could be seen in the process of desquamation from the alveolar walls. These were more elongated, and had a simple round or oval nucleus. The older and larger forms often showed either no nucleus or a remnant of one, and often contained pigment. Some of the alveoli contained coarsely arranged fibrin. In places the alveolar septa were either absent or ruptured. Few extracellular Gram-negative bacilli were seen. No organisms were noted within the polymorphonuclear forms.

Sections taken from isolated nodular areas showed similar findings. More red blood cells were found within the spaces, and the capillaries were often markedly dilated.

Case III (Med. No. 2249).—Patient was a letter-carrier, aged fifty-nine years. He had a marked alcoholic history. For many years he had complained of stiffness in his joints. Thirteen days before admission to the hospital, following an exposure to cold, he complained of swelling and tenderness of various joints of his hands. These were inflamed and showed evidences of an acute inflammatory condition. One week later his condition subsided, but the patient gradually became comatose and delirious. His temperature at this time was subnormal, his pulse 84, his respirations very slow and Cheyne-Stokes in type. He was admitted to the hospital in this condition.

Physical examination showed an elderly, emaciated man. There were extreme contractures and enlargements of various joints. The auricles of both ears were filled with tophi. Thorough examination was very unsatisfactorily carried out, owing to the patient's comatose condition, but was apparently essentially negative, except for the deformities involving the joints. The blood-pressure was 110. The muscles of the arms and hands contracted intermittently. Two days after admission the respirations became accelerated, 30 per minute, the temperature reached 100, the pulse varied from 80 to 110, and for the first time a few rales were heard at the bases of the lungs. There was no cough, no sputum, little cyanosis. Death occurred three days after admission to the hospital.

Clinical Pathology. Urinary examination showed a slight trace of albumin and many granular casts. There was slight secondary anemia. White-cell count 6000 at entrance. Urea nitrogen 66.5 mgs. (per 100 c.c. of blood).

The spinal fluid was under increased pressure, otherwise normal. Stool examination showed normal findings.

Autopsy, A–15–9. . The autopsy was performed five hours after death. The arthritic changes were those associated with gout. Of special interest was the condition of the lungs and kidneys. The combined weight of the latter was 110 grams. The capsule stripped fairly easily, leaving a warty verrucous surface. The findings on section were those of a small contracted kidney. This was also confirmed by microscopical examination.

The pleural cavities contained no free fluid; there were no adhesions. The left lung weighted 380 grams, the right 1090 grams. Except for slight evidence of congestion the findings in the left lung were unimportant. The right lung, on the other hand, was voluminous and completely filled the pleural cavity. The lower two-thirds of the superior lobe, the portion adjoining the hilus of the middle lobe, and the entire inferior lobe, were dark red in color and were completely consolidated. There was a finely granular, fibrinous exudate over the pleural surface of these portions of the lung. The pleura over the apex was gray and greatly thickened. The tissue beneath, however, was crepitant. The lower two-thirds of the middle lobe presented a wavy, emphysematous, light pinkish-gray appearance. Over the middle third were a few isolated, raised, slightly injected areas. These were nodular and firm. Cross-section of the superior lobe presented an upper portion corresponding to the apex that showed normal lung markings. Adjoining this and poorly demarcated from it the tissue was gray to pink in color and had a fleshy appearance. The surface was definitely granular, and there was present a small amount of sanguinous, slightly mucoid exudate. This could be scraped off without removal of the parenchyma. The alveolar spaces were completely obliterated. Portions of the consolidated areas sank in water. The surface of the proximal third of the middle lobe presented a similar appearance. The parenchyma adjoining the consolidated portion was greatly injected. Focal gray areas, about 1 cm. in diameter, surrounding by an injected margin, were scattered through the middle third. On cross-section of the inferior lobe the surface presented a more bizarre appearance. It cut with increased resistance. The lower portions were very dark red in color, the middle and upper gray. There was a gradual blending between the two. The exudate here was granular, slightly mucoid, but not abundant. Alveolar structures could not be made out along the lower margins. Although the surface had a mottled appearance, this was apparently not due to a lobular distribution of the process. The areas of grayer consolidation were softer than the more injected ones.

Microscopic Findings. Sections were taken from various portions of consolidated lung tissue and stained with methylene blue and eosin and by Gram's method. These all showed essentially the same characteristics. The alveoli were markedly dilated and completely filled with an exudate composed chiefly of polymorphonuclear cells. Associated with these was a relatively large amount of coarsely trabeculated fibrin and granular material. There were also encapsulated bacilli, exclusively Gram-negative. Some of these appeared as oval cocci, others as more elongated forms, occurring singly or in pairs. The majority of the organisms were intracellular. They varied somewhat in numbers in the different sections, but never constituted a large part of the exudate. Rare large vacuolated cells containing pigment and organisms were seen. The demarcation between the alveoli filled with exudate and those more normal in appearance was not sharply defined. The capillaries of the septal walls were often dilated and contained red blood cells. These were found in the exudate in small numbers. Cultures taken from lung (consolidated portion), spleen, and liver all showed a pure growth of the Bacillus mucosus capsulatus.

Case IV (Med. No. 661).—This patient was a chauffeur, aged thirty-one years, who developed pain in the left side of the chest six weeks before admission to the hospital. Two thoracocenteses were performed by his local physician and gave negative results. The physical signs on admission were those indicating fluid in the left chest, with a right lateral cardiac displacement. The chest was tapped and later drainage established. Some days later a bronchial fistula developed. The material recovered at operation consisted of 1300 c.c. of greenish-yellow, mucoid fluid, purulent in appearance, and very foul smelling. An organism corresponding to the Bacillus mucosus capsulatus was found in pure culture in this pus. The patient, who previously had been febrile, soon became afebrile, the white-cell count returned from 14,500 to normal, the subjective symptoms disappeared, and recovery was apparently complete three months after discharge from hospital.

Bacteriology. The organisms we are dealing with in each of these cases undoubtedly are identical. In all four cases the smears from the lung exudate showed rod-like organisms of variable length. Sometimes they were short and could easily be mistaken for cocci with the ordinary stains. The rods often measured 3μ in length. They occurred either in short chains or singly. The ends were definitely rounded. A capsule could easily be demonstrated in smears from tissue by Welch's stain or by treating the preparation for a few seconds with a dilute solution of formalin, stained with gentian violet and mounting either in salt solution or balsam. The capsule could be demonstrated also in smears of organisms from culture media. The organisms did not stain by Gram; they were non-motile.

The cultural characteristics of the organisms as found in Cases I, II, and III were as follows: (Unfortunately those of the organism in Case IV were not exhaustively studied.)

1. Plain agar, after twenty-four hours at 37° C., showed a profuse growth, slimy, somewhat translucent, almost colorless. The colonies rapidly coalesced and soon became whitish in color. Cultures remained viable for four weeks and longer at room temperature.
2. Bouillon: this became very cloudy within twelve to fourteen hours, and a mucoid mass was often found at the bottom of the tube.
3. Gelatin showed the typical knob-like growth at the surface in stab culture. The gelatin was not liquefied.
4. Potato: a white to yellowish-gray, mucoid growth appeared in twenty hours at 37° C.
5. Blood serum: after twenty-four hours at 37° C. showed a very profuse translucent, mucoid colorless growth.
6. Litmus milk: this was not coagulated in cultures from Cases I and II; however, coagulation took place in cultures from Case III. The smears made from these cultures showed capsular formations more easily than those from other media.
7. The organisms did not produce indol in pepton-solutions.

Pathogenicity. Twenty-four hour bouillon cultures taken from the lung exudate injected intraperitoneally (1 to 2 c.c.) into guinea-pigs killed the animals in from twelve to twenty-four hours. The lesion found was invariably a peritonitis. The peritoneum was completely covered by a profuse, moist, colorless, slimy exudate, containing few polymorphonuclear cells and numerous encapsulated bacilli. No deposition of fibrin was noted.

DISCUSSION. The three cases recorded above illustrate points that seem worthy of special consideration. Attention has previously been called to the rapid course of this form of pneumonia. Case I died thirty-one and a half hours after the first onset of symptoms, and in less than twenty-four hours after the patient went to bed. This represents the shortest duration of this infection recorded in the literature. This fact bears some significance. It not only shows the extreme severity of the disease, but also gives added confirmation to the idea repeatedly set forth that there is a form of pneumonia, *sui generis*, caused specifically by the Bacillus mucosus capsulatus. It seems quite improbable, in consideration of the short duration of the illness, to assume that another organism caused the pneumonia and that the Bacillus mucosus capsulatus was a secondary invader. The chills associated with the onset of the illness in this case were apparently unusual. Aided by the positive blood culture taken before death, the diagnosis was correctly made clinically. In practically all of the reported cases the diagnosis has been made at autopsy. The fact that pure cultures of the bacillus were found in the sputum, in the heart's blood, antemortem and postmortem, and from smears from the lung exudate, confirms the supposition that we are without doubt dealing with a case of so-called "Friedländer pneumonia." The early appearance of the lesion is of special interest from a pathological point of view. The more hemorrhagic condition, the lobular distribution, with a tendency to become confluent, and the large number of organisms within the alveoli, are all striking features.

In Case II the exact diagnosis of the condition was not made clinically. A blood culture might have been of value, although late in the disease this is usually negative. No mention is made of the presence of bacilli in the sputum, although cocci were numerous. In view of the pathological findings these undoubtedly were the Friedländer organisms. It is of interest in this connection to remember that Friedländer first described the organism as a "micrococcus," and that Sternberg considered the pneumococcus identical with the Bacillus mucosus capsulatus. That the presence of the Friedländer organism in the sputum is not necessarily indicative of a pneumonic process, has been pointed out by Smith and others. It occurs in many other conditions in the sputum, but always in fewer numbers than in cases of Friedländer pneumonia. The macroscopic lesions in the lungs afford a contrast to those seen in Case I. The gray, almost white appearance of the tissue, the tendency to become necrotic and form cavities, were striking features. Here the exudate within the alveolar spaces contained fewer organisms than in Case I. The large vacuolated cells found in the alveolar exudate were more numerous than in the preceding case.

The exact duration of the disease in Case III cannot be determined. The patient on admission, three days previous to death, although *in extremis,* showed on physical examination normal pulmonary findings. The pneumonia was a terminal condition in a case of advanced gout and chronic nephritis. The sudden onset and the evident short duration of the disease are striking features. The presence of a pneumonia had not suggested itself to those in charge of the patient. This is only in part explained by the extreme condition of the patient and the difficulty of thorough examination. From a pathological point of view the findings are of interest because of the absence of any definite characteristic features. The lesions macroscopically and microscopically were essentially identical with those of any pneumococcus pneumonia. Indeed, the possibility of a Friedländer pneumonia was suggested at the autopsy, but thought improbable because of the small amount of mucoid exudate. The lung, as seen at autopsy, represented a lobar distribution of the process. This may possibly have been caused by the confluence of rapidly developing foci of bronchopneumonia. In contrast to the foregoing cases there were notably few large phagocytic vacuolated cells in the exudate. As in Case II early foci of necrosis were found. The pathological diagnosis was made essentially on the presence of the "pneumobacilli" within the alveolar spaces. Although these were the only organisms found, as in Case II, the duration of the disease was so long that an initial infection in each case with some other organism cannot be absolutely excluded.

Case IV represents one of the few cases of Bacillus mucosus capsulatus infection that recovered. Apelt and Philippi each have reported similar cases. These were associated with other organisms. In Case IV it seems probable that the Friedländer bacillus was the important factor in producing the pathological process. The large number of organisms present, the bronchial fistula, and cavity formation also support this view.[31]

SUMMARY. Based upon the reports of cases thus far assembled in the literature, and upon the study of the cases here recorded, it is possible to deduct certain characteristics of this form of infection. It occurs in 5 to 10 per cent. of all cases of pneumonia, considering it both as a primary and secondary invader. It is primarily a disease of late adult life. It seems very remarkable that but one case of so-called "Friedländer pneumonia" has thus far been found in infants and children, where pulmonary infections are so common. Although the disease is subject to great variation in its clinical course, the duration is characteristically short. The onset may or may not be associated with a chill. Some emphasis has been placed upon the absence of the chill in this form of pneumonia, making this somewhat characteristic of the disease. This consideration does not seem to us to be of much importance. Herpes labialis certainly is found less commonly in association with this form of pneumonia than with the usual pneumococcus form. The signs of toxemia in this disease are profound. General weakness, coma, signs of cardiac and respiratory failure all come suddenly and are outspoken. The frequency of the various lobes involved is of little importance. The outcome is apparently always fatal, death coming often with little premonition. It seems conceivable, especially in children, that the disease may exist, be unrecognized as this form of pneumonia, and be followed by recovery. Of importance from a clinical-pathological point of view is the sanguineous, very slimy, non-purulent, voluminous sputum, in which the organisms are found to occur in great numbers. In this connection, as pointed out above, the Bacillus mucosus capsulatus is often found in the sputa of individuals not suffering from pneumonia, although rarely in so great numbers. The identification of the organism in the blood antemortem is of great diagnostic importance. Although the temperature oftentimes is not as high as is found in many types of pneumonia, and the pulse relatively low, these facts have little diagnostic significance.

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[31] When this case (IV) was first studied it was considered a pulmonary condition, associated with the Bacillus mucosus capsulatus, that recovered. More recent developments, however, show clearly that there was also a tuberculous process present, for tubercle bacilli have been very recently found in the sputum. There are many cases reported in the literature in which the Friedländer organism is found together with the tubercle bacillus.

From a pathological point of view there is no one feature that distinguishes this form of pneumonia from the pneumococcus lobar type. Certain characteristics, however, taken together make the process comparatively easy to recognize. In general we can say that the initial process has a tendency to have a lobular distribution. This is seen in the mottled, marble-like appearance of the lung. Later stages of the disease tend to definite lobar distribution, and are followed by characteristic abscess formations and necrosis of the lung parenchyma. The tissue at this stage has a very peculiar grayish-slaty color. The lung exudate so often referred to in the literature is copious, slimy, mucoid in character. It is to be borne in mind that this is not pathognomonic and is entirely dependent upon the numbers of organisms present.

Histologically the exudate generally contains very numerous capsulated bacilli, which are both extracellular and intracellular. Alveoli may be completely filled with organisms; again, polymorphonuclear cells may be more numerous. The demarcation in one field between alveolar spaces that are infiltrated with an exudate and those that appear normal is often striking. The large vacuolated phagocytic cells are more numerous, also more phagocytic, in this type of pneumonia. The histogenesis of these cells must remain in doubt until better methods of cell differentiation are at our service than the purely morphological. From the findings in our cases we have regarded them as most probably due to proliferation of the alveolar epithelium.

Conclusions. 1. There exists a type of lobar pneumonia, *sui generis,* that is caused by the Bacillus mucosus capsulatus.

2. Clinically this so-called "Friedländer pneumonia" is subject to great variation.

3. The exact diagnosis is difficult to make clinically, but is aided by the identification of the Friedländer bacillus, both in the blood and sputum.

4. The pathological findings, taken together, are usually quite typical for this form of pneumonia.

OBSERVATION UPON THE ELIMINATION OF ACETONE AND DIACETIC ACID IN TWO HUNDRED AND FOURTEEN SURGICAL CASES.

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AND

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In Dr. Crile's recent work upon shock and the application of anoci-association, he draws attention to the concentration of the H ion in the blood of dying persons and those in the state of surgical shock or fatigue in general. It may be of interest to notice the elimination of persons suffering from various surgical conditions, with reference to the output of acetone and diacetic acid in the urine and the amount of shock present.

In studying 214 consecutive surgical patients in Dr. John B. Deaver's service at the German Hospital it was immediately noticed that acetone was eliminated in a large percentage of cases (85 per cent.), with but little reference to the objective condition of the patient, the severity of the pathology, and the gravity of the operation; also that the more emotional, frightened, or anxious individuals invariably were the more shocked and also showed the more acetone. Diacetic acid was less frequently met with (17 per cent.), and then only several days after the operation, and in women showing large outputs of acetone. (Men, diacetic acid negative; women, diacetic acid 38 per cent.) 8.8 per cent. had acetone on admission and 23.3 per cent. on the morning before operation. Here again the instances were chiefly with the more neurotic and anxious.

Ether was the anesthetic in all but four cases where Dr. Crile's principles of anoci-association, with NO_2 anesthesia, were followed. One of these latter, a thyroidectomy for exophthalmic goitre was among the 15 per cent. without acid elimination at all.

The elimination of acid bodies ceased in very many instances by the third day after operation, and in all but 3 per cent. by the day of discharge after the patient had been up and about the ward for several days.

"Starvation," namely, constant saline by bowel and nothing by mouth, was nearly always accompanied by more acetone elimination.

Sex seemed to play some part, for of the 79 male patients observed, 2 showed acetone on admission and 3 on the morning of operation; while of the 135 female patients, 17 were eliminating acetone when admitted and 49 on the morning of operation. Also all of the 38 instances in which diacetic acid was eliminated were found among the women.

A brief tabulation of the statistics is as follows:

Chronic Appendicitis. 48 appendectomies; 4 per cent., no acid at all.

On admission	Acetone	4 per cent.	Diacetic	negative.
Day of operation	"	27 "	"	"
First day after operation	"	70 "	"	"
Second day after operation	"	90 "	"	"
Third day after operation	"	30 "	"	"
On discharge	"	negative.	"	"

Chronic Appendicitis. Complicated by laceration of cervix and perineum; pregnancy; retroversion of uterus; anteflexion of uterus; chronic salpingitis, oöphoritis and endometritis; abdominal adhesions; fissure-in-ano; fistula-in-ano; hemorrhoids—17 cases; 6 per cent. showed no acid.

On admission	Acetone	12 per cent.	Diacetic	negative.
Day of operation	"	12 "	"	negative.
First day after operation	"	78 "	"	6 per cent.
Second day after operation	"	48 "	"	12 "
Third day after operation	"	6 "	"	negative.
On discharge	"	negative.	"	negative.

Acute Appendicitis. 8 cases; all showed acid.

On admission	Acetone	25 per cent.	Diacetic	negative.
Day of operation	"	37 "	"	negative.
First day after operation	"	75 "	"	25 per cent.
Second day after operation	"	100 "	"	25 "
Third day after operation	"	50 "	"	25 "
On discharge	"	12.5 "	"	negative.

Exophthalmic Goitre. 4 cases; 1 showed no acid (anoci-association).

On admission	Acetone	negative.	Diacetic	negative.
Day of operation	"	25 per cent.	"	negative.
First day after operation	"	75 "	"	25 per cent.
Second day after operation	"	75 "	"	25 "
Third day after operation	"	25 "	"	negative.
On discharge	"	negative.	"	negative.

Operations of a minor surgical character for labial cyst; lacerated cervix and perineum; chronic endometritis; incomplete abortion; thoracic empyema; abscess of abdominal wall; lipomata; fibromata; epitheliomata; shortening of the round ligaments in inguinal canal; removal of bone plates; abdominal adhesions, 20 cases; 15 per cent. showed no acid.

On admission	Acetone	5 per cent.	Diacetic	negative.
Day of operation	"	30 "	"	negative.
First day after operation	"	60 "	"	10 per cent.
Second day after operation	"	55 "	"	10 "
Third day after operation	"	20 "	"	negative.
On discharge	"	negative.	"	negative.

Hemorrhoids. 6 cases; acetone negative on admission; all showed acetone on day of operation, 3 on second day, 2 on third day, and negative on discharge.

Hypertrophied prostrate (suprapubic prostatectomy). 2 cases; acetone negative on admission; both showed acetone for two days after operation, one on third day, negative on discharge.

Herniæ. 1 ventral, 2 umbilical, 5 femoral, 17 inguinal, 5 herniorrhaphy with appendectomy, 1 with posterior gastro-enterostomy, 31 cases; all showed acid.

On admission	Acetone	4 per cent.	Diacetic	negative.
Day of operation	"	4 "	"	"
First day after operation	"	20 "	"	"
Second day after operation	"	30 "	"	"
Third day after operation	"	20 "	"	"
On discharge	"	negative.	"	"

Operations of a major surgical character for carcinoma of pancreas; submucous fibroids (hysterotomy); double pyosalpinx; intraligamentary abscess; chronic cholecystitis; acute cholecystitis; chronic pancreatitis; cholelithiasis (cholecystostomy, cholecystectomy, choledochostomy); ventral hernia with cholelithiasis; myoma uteri; ovarian cyst; hysterectomy (complete or supravaginal amputation); hysterotomy (for placenta previa, premature separation of placenta, submucous fibroid, chronic endometritis or diagnosis); twisted ovarian cysts or subserous myomata; nephrectomy (tuberculosis or pyonephrosis); posterior gastro-enterostomy (carcinoma or ulcer); carcinoma of colon (resection or exclusion); ectopic pregnancy (ruptured and unruptured), 65 cases; 3 per cent. showed no acid.

On admission	Acetone	22 per cent.	Diacetic	4 per cent.
Day of operation	"	57 "	"	4 "
First day after operation	"	90 "	"	12 "
Second day after operation	"	84 "	"	15 "
Third day after operation	"	48 "	"	12 "
On discharge	"	12 "	"	6 "

Breast (radical amputation for carcinoma; simple amputation for adenofibroma), 5 cases. One case showed no acid (carcinoma);

1 case had acetone on admission; 1 on day of discharge; 3 on first day; 1 on second day; 1 on third day; negative on discharge. None showed diacetic acid.

The relation of the acid elimination to the amount of shock observed was far from constant. The following four tables will show:

1. Ten instances in which the objective shock was considerable; many patients had to receive intravenous saline and active stimulation for some hours after operation, but eliminated a relatively small amount of acid bodies.

Acute Cholecystitis and Pancreatitis. Acetone positive on day of operation.

Cholelithiasis and Umbilicial Hernia. Acetone positive for two days after operation.

Abscess of Broad Ligament. Acetone positive on day of operation and for two days afterward.

Double Pyosalpinx, Myoma Uteri, and Acute Appendicitis. Acetone positive on day of death, ten days after operation.

Abscess of Left Broad Ligament. Acetone positive on admission, day of operation, and first day after.

Acute Appendicitis. Acetone positive for three days after operation.

Ectopic Pregnancy. Acetone positive day after operation.

Carcinoma of Sigmoid (resection and sigmosigmoidostomy). Acetone negative throughout.

Acute Cholecystitis. Acetone positive on day of operation and for two days after.

Cholecystectomy (*cholelithiasis*). Acetone positive for two days after operation.

On admission	Acetone	20 per cent.	Diacetic	negative.
Day of operation	“	50 “	“	“
First day after operation	“	80 “	“	“
Second day after operation	“	60 “	“	“
Third day after operation	“	10 “	“	“
On discharge	“	negative.	“	“

(Death, 1 instance, or 10 per cent.).

2. Ten instances in which the elimination of acetone and diacetic acid was remarkably high, calling attention to the type of surgery.

Chronic Appendicitis. Acetone positive day of operation and first, second and third day after operation. Diacetic acid positive first and second day after operation.

Acute Appendicitis and Cholelithiasis. Acetone positive on admission, day of operation and for three days after operation. Diacetic acid on second day.

Myoma Uteri (*supravaginal amputation*). Acetone positive day of operation and for three days after operation.

Retroversion of Uterus (*suspension*). Acetone positive on day of admission, day of operation, and for three days after operation. Diacetic acid positive for two days after operation.

Ovarian Cyst (small). Acetone positive day of operation and for three days after operation. Diacetic acid positive third day after operation.

Myoma Uteri (complete hysterectomy). Acetone positive for three days after operation and on day of discharge. Diacetic acid positive second and third day and on discharge.

Tuberculosis of Kidney. Acetone positive day of operation and for three days after operation. Diacetic acid positive for three days after operation.

Cholelithiasis (cholecystectomy and choledochostomy). Acetone positive on day of admission, day of operation, three days after operation, and on discharge. Diacetic acid positive for three days after operation.

Hysterotomy. Acetone positive day of operation, for three days after operation, and on discharge. Diacetic acid positive two days after operation.

Pyosalpinx (left). Acetone positive for three days after operation. Diacetic acid positive second day after operation.

On admission	Acetone	30	per cent.	Diacetic	negative.	
Day of operation	"	80	"	"	negative.	
First day after operation . . .	"	100	"	"	50	per cent.
Second day after operation . . .	"	100	"	"	80	"
Third day after operation . . .	"	100	"	"	40	"
On discharge	"	30	"	"	10	"

3. Ten instances selected for their small amount of acetone elimination, again noticing that the surgery ranged from a simple appendectomy to complete hysterectomies and hysterotomies. Colon resection and common-duct drainage cases.

Chronic Appendicitis. Acetone positive on day of operation.

Pyosalpinx (right) and Retroverted Uterus. Acetone positive first and second day after operation.

Lacerated Cervix and Fissure-in-ano. Acetone positive first day after operation.

Chronic Appendicitis, Double Ovarian Cyst, Ventral Hernia, and Lacerated Cervix and Perineum. Acetone positive on first day.

Myoma Uteri (complete hysterectomy). Acetone positive second and third day after operation.

Acute Suppurative Pancreatitis (cholecystectomy and choledochostomy). Died. No acid eliminated.

Thoracic Empyema. Acetone first day after operation.

Cholelithiasis (cholecystectomy and choledochostomy). Acetone positive on second day.

Cholelithiasis (cholecystectomy and choledochostomy). Acetone positive on first day.

On admission	Acetone	negative.		Diacetic	negative.
Day of operation	"	10	per cent.	"	"
First day after operation . . .	"	40	"	"	"
Second day after operation . .	"	40	"	"	"
Third day after operation . . .	"	10	"	"	"
On discharge	"	negative.		"	"

4. Ten instances of the most shock observed in the entire 214 cases and the comparison to the elimination of acetone and diacetic acid.

Cholelithiasis and Acute Pancreatitis. Acetone positive on first day after operation.

Cholecystitis (*cholecystectomy and choledochostomy*). Acetone positive on day of admission, day of operation, and three days after operation. Diacetic acid positive for two days after operation.

Tuberculosis of Kidney (*nephrectomy*). Acetone positive on day of operation, for three days after operation, and on discharge. Diacetic acid positive for three days after operation.

Myoma Uteri (*supravaginal amputation*). Acetone positive for three days after operation and on day of discharge. Diacetic acid positive second and third days after operation and on discharge.

Acute Suppurative Pancreatitis (*cholecystectomy and choledochostomy*). Died. No acetone.

Cholelithiasis and Myocarditis. Acetone positive on admission, day of operation, and two days after operation.

Hysterotomy. Acetone positive for three days after operation. Diacetic acid positive day after operation.

Acute Appendicitis, Cholelithiasis, Myoma Uteri, Ovarian Cyst (*right*). Acetone positive on admission, day of operation, and for three days after operation. Diacetic acid positive on second day after operation.

Carcinoma of Breast. Acetone positive on day of operation.

Cholelithiasis (*cholecystectomy*). Acetone positive for two days after operation.

On admission	Acetone	30	per cent.	Diacetic	negative.
Day of operation	“	50	“	“	negative.
First day after operation . . .	“	80	“	“	30 per cent.
Second day after operation . . .	“	70	“	“	40 “
Third day after operation . . .	“	50	“	“	20 “
On discharge	“	20	“	“	10 “

In the seven instances where death terminated, the record (3.2 per cent.), the extreme shock, and fatal outcome, together with the slight elimination of acetone and conspicuous absence of diacetic acid, form an interesting feature. The statistics were as follows:

Suprapubic Prostatectomy (*followed by gangrene of bladder and death from toxemia*). Extreme shock after operation; showed acetone only on second day after operation, with a faint trace on the third day, after which urine was negative.

Resection of Cecum and Entire Colon. With first part of sigmoid and two feet of terminal ileum for carcinoma; ileosigmoidostomy; extreme shock; died. Acetone negative.

Cholecystoduodenostomy. For carcinoma of pancreas. No shock following operation. Death from bronchopneumonia. Acetone positive on second day only.

Acute Pancreatitis. With choledochostomy and cholecystostomy. Moderate shock. Death from toxemia. Acetone negative throughout.

Resection of Cecum and Ascending Colon. For carcinoma. Ileocolostomy. Moderate shock. Acetone positive for two days after operation; faintly positive third day.

Cholelithiasis and Myocarditis (with cholecystectomy and choledochostomy). Extremely shocked. Died from cardiac failure. Acetone faintly positive on admission, on day of operation, and strongly positive on day after operation, then negative until death.

Gangrenous Appendix, Double Tubal Abscess, and Myoma Uteri. Appendix, uterus, tubes and ovaries removed. Greatly shocked. Lived for ten days with large draining wound. Acetone positive only on day of death.

In no one of the seven instances was diacetic acid found, and in only one was acetone found after the third day.

CONCLUSIONS. In summing up the above statistics it can only be said:

That acetone occasionally accompanied by diacetic acid was eliminated in the urine of 182 out of 214 consecutive surgical patients (in 23.3 per cent. before surgical intervention and in 61.7 per cent. after operation, under ether anesthesia).

That the temperament of the individual and the length of time pre-operative treatment (of nothing by mouth and saline by bowel) had been carried out, appeared to have a slight positive effect upon the acetone eliminated.

That acetone and diacetic acid were eliminated oftener and in larger quantities in women than in men.

That the fact of surgery alone increased the acid, but the severity of the operation and the amount of obviuos shock present had but little bearing upon the amount of eliminated acid and the time of elimination.

These statistics have been compiled through the courtesy of Dr. John B. Deaver from his various services at the German Hospital, and acknowledgment is made by the writers.

LUETIC ARTHROPATHIES.[1]

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THE progressive differentiation of diseases has played a fundamental part in the development of medicine, and the hope of contributing to it has been a stimulus to conscientious workers. Its influence on the evolution of medical thought has gone far toward breaking the ties of charlatanism and separating medical science from the so-called healing art of the earlier centuries. Our conceptions of diseased conditions have recently broadened with an unprecedented rapidity; with the advent of newer discoveries medical men of today are able to solve many of the problems which wholly baffled our predecessors. The application especially of the advances made along the lines of physical, chemical, and biological investigation has enabled us to simplify our classification of diseases and to establish a more definite etiological basis for many of them. As Cabot so aptly remarks, "To classify cases of disease according to their pathogenic agent and not solely by naming the region affected or the function disturbed is the ideal of scientific progress in medicine." The recognition of the protean manifestations of syphilis is a striking example of this point. Since the brilliant discoveries of Schaudinn and Hoffmann, in 1905, and the classical work of Wassermann and others on the biological characteristics of the Treponema pallidum, its secret haunts have been exposed to the eye of careful observers. Thus, syphilitic involvement of the joints has in recent years been attracting the attention of the internists, and many luetic arthropathies formerly obscure have been cleared up and more rational treatment instituted, due largely to these studies.

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[1] Read before the Richmond Academy of Medicine, January 12, 1915.

Although the text-books practically ignore the Treponema pallidum as a not infrequent etiological factor in certain types of arthritis, it is interesting to find that such syphilitic diseases of the joints were recognized as early as the fifteenth century. The writings of Petrus Martyr, in 1448, Alphonsus Ferrus, in 1537, and Morgagni, in 1600, contain references to such conditions, but it is interesting to know that Hunter was strongly opposed to the views of those authors. It was not until 1853 that the first clear case of luetic arthropathy was accurately described by Richet. Its infrequency, or the failure of its recognition, is indicated by the fact even as late as 1882 Zeissl diagnosed only one case of syphilitic joint involvement in a series of one thousand syphilitics. Since then the literature of the subject has become voluminous; most articles, deal, however, chiefly with isolated or with only short series of cases. Most of the reports antedate the advent of the Wassermann reaction, so doubtless many errors of omission and commission were made. In spite of the comparative frequency of luetic infection of the joints, it is remarkable to find how meager is the general knowledge on the subject, as is reflected in our American text-books. Exhaustive treatises on this subject are to be found in the German and French archives only. Thus Fournier asserts that 39 per cent. of all congenital syphilitics have arthritis, and von Hippel, 56 per cent., while Schuller says that 7 per cent. of all joint diseases in children are syphilitic. Tubby places similar infections of the bones and joints second in frequency only to the Hutchinson triad in his congenital cases. Levine believes that hereditary and acquired joint syphilis are far more common than they are generally thought to be, and Baets reports that out of 100 cases of arthritis in the Canal Zone, 63 were syphilitic. The pediatricians more than the internists have been keenly alive to the congenital luetic arthropathies in infants and to the recognition of spirochetal infection of an acquired nature. Undoubtedly, numbers of both acute and chronic arthritides of specific origin have passed through medical hands unrecognized. O'Reilly, in a comprehensive article on the subject, believes that a consideration of a possible luetic etiology should play an important role in the diagnosis of any type of joint involvement, while Skillern feels that every atypical case of arthritis should be subjected to a complement-fixation test.

My interest in this subject was stimulated by a study of a patient with the following history:

Male (white; merchant), aged forty years, presented himself complaining of "rheumatism."

His *family history* was unimportant. In his past history his health had been entirely good with the exception of some pain in his joints, which, however, never became acute. About eight years previous to his present trouble a diagnosis of "soft chancre" had been made by his attending physician. No treatment was given and apparently no ordinary clinical manifestations of lues appeared subsequent to this period. He denied gonorrheal infection.

The onset of his present illness was marked by general malaise, sore throat, and dull, aching pains through the body. Within a few days his throat became progressively more tender and the bodily pain became localized in his shoulders, right elbow, and left knee. Later his left foot, including the ankle and toes, became involved. These various joints were so exquisitely tender that even the weight of the bed-clothes was uncomfortable.

Physical examination showed a well-nourished man with rather flushed skin and profuse perspiration. The eyes were normal, the pupils reacting to light and to accommodation.

The throat showed rather large tonsils for an adult, much inflamed but not ulcerated. His teeth were in good condition. The lungs were normal on percussion and on auscultation. His heart was uniformly enlarged, the deep dulness extending one fingerbreadth lateral from the left nipple line in the fifth interspace and just beyond the sternal border on the right in the fourth interspace. The sounds were clear with the exception of an exaggerated aortic second sound. Blood-pressure 180 (systolic). Pulse 100, regular, and of full volume. Temperature 102°.

Abdomen negative. Liver and spleen not felt. Genitals negative. Extremities: reflexes normal. The skin over the left shoulder was red, tense, and hot. Motion caused great pain. As well as could be determined there was no increase in intracapsular fluid. The other affected joints presented much the same picture.

His urine was pale, of low specific gravity, and showed a cloud of albumin with hyaline and granular casts. No sugar was present. His blood showed a leukocytosis of 12,000.

The diagnosis of acute rheumatic fever was made and the usual treatment was instituted. After the administration of the salicylates and their accompaniments for one week his condition was not improved: in fact, it was growing progressively worse. During this period his temperature varied from 99.5° to 102.5°, and his affected joints could not be touched without exciting pain and his throat continued sore. Finding that his blood gave a positive Wassermann test at this time, mercury and iodide were immediately begun. The effect was remarkable: the fever rapidly subsided, his joints cleared up, but his blood-pressure and urinalysis remained the same. As far as could be determined there was no joint residue.

My interest was further heightened by a patient whom Dr. W. B. Porter referred to me for a Wassermann test with a provisional diagnosis of syphilitic arthritis. His history is as follows:

Male (white; farmer), aged thirty-seven years. His chief complaint was stiffness, swelling, and soreness of his joints.

His family history was negative and his past history was unimportant, with the exception of a record of a chancre appearing sixteen days after intercourse twelve years ago. Glands appeared in his groin at that time, but he remembered no secondaries. He was given a short treatment, ceasing with the disappearance of the primary lesion. He married subsequently and both his wife and children have been in good health. His general health has always been normal aside from his joints.

His present illness began eleven years ago with stiffness and swelling in both knees, later involving progressively other joints. With the disappearance of the swelling there was never any residue, and he was never confined to bed. At times he was free from symptoms for a period of six to eight months. During recent years his shoulders, elbows, and finger-joints have become involved to a more marked degree, so that he has not been at work for eighteen months.

Physical Examination. Throat and eyes negative. Teeth carious and gums spongy.

Funnel-shaped chest. Heart displaced to left, probably due to the deformity. Sounds clear. Lungs clear.

Abdomen negative. General glandular enlargement. Reflexes normal.

Extremities: Swelling, stiffness, and partial ankylosis of left elbow. Right elbow stiff and swollen to less extent. The second phalangeal joints of both hands were enlarged, stiff, and tender; the patient was completely unable to flex either hand.

Both knees were tender to pressure, but they showed no swelling or stiffness.

Blood-pressure 120 systolic and 78 diastolic. Temperature 98°.

Urine negative. Blood normal, with the exception of a positive Wassermann.

None of the affected joints showed signs of fluid, but there was definite resistant synovial thickening about them.

This patient was given four doses of "606" followed by potassium iodide and mercury. His improvement began after the second dose, and has been progressive. All signs have cleared up except a slight ankylosis in his left elbow. He has been at work continuously for six months, previous to which time he was more or less incapacitated for any form of labor.

Impressed by the dissimilarity of these cases of the same infectious origin, I thought it would be of interest to make a somewhat exhaustive study of syphilitic arthropathies, and to record the different types as described by the various observers. It is needless to add that one finds it difficult to confine the manifold manifestations of syphilis to a rigid classification, but for practical purposes the more general forms can be catalogued. A further difficulty encountered is the lack of a uniform terminology for joint affections. Fortunately the leaders in modern medicine are rapidly overcoming this impediment and are paving the way for a more definite understanding of these conditions. Another source of error or of difficulty in the diagnosis and classification of these cases lies in the fact that improper deductions may be made from a positive Wassermann test in certain arthritic patients. Just as we feel that many syphilitic arthritides were not recognized by the older writers, we must admit the possibility of a positive Wassermann misleading us in those cases in which the coexistence of syphilis has no bearing upon the joint process.

1. ARTHROPATHIES OF CONGENITAL LUES. The types of hereditary joint syphilis are better known and, as stated by O'Reilly, are more frequent than the acquired forms. According to Tubby, this class of affections is secondary to a contiguous bone syphilis. Naturally the symptomatology of such bone involvements is not unlike that of an arthritis, and may therefore conveniently be included under this heading.

(*a*) *Osteochondritis syphilitica*, first described by Wegner, is highly characteristic of congenital lues. According to Whitman, "There is a multiplication and irregularity of the cartilage cells of the ossifying layers and premature calcification. As a result, the circulation is insufficient, and necrosis of a part of the cartilage may follow, which, acting as a foreign body, sets up inflammatory changes in the adjoining parts. The process is shown by a zone of hard, dry, yellow substance in the ossifying layer, adjoining which is an inflammation of the tissues of the newly formed bone, which is the part replaced by granulation tissue. If the disease is progressive, ulceration and suppuration may follow, the cartilage may be destroyed, and the epiphysis may be separated, causing deformity and cessation of growth. The neighboring joint is usually involved. In the milder cases there is a simple sympathetic synovitis; in the advanced class a destructive arthritis." Parrott claims that this is the most common type, affecting, as a rule early infancy. Painful sensitive swellings appear at the epiphyseal junctions, either as small hard tumors or as general enlargements circumscribing the joint, and is soft and boggy and helpless. Taylor, on the other hand, believes that joint involvement in this type is exceptional only when the epiphysis is narrow and contiguous with the synovial membrane. In untreated cases the picture changes simulating acquired lues, giving rise to periostitis, osteitis, and a more or less typical synovitis.

(*b*) *Simple synovial effusion* as described by Clutton rivals the former disease in frequency. Appearing generally in children from eight to fifteen years of age, it is usually symmetrical, painless, and with no impairment of motion (Patton). The knees are commonly involved. It is frequently associated with keratitis. In some cases considerable fluid can be demonstrated, though, as a rule, it is moderate in amount. Tubby feels that this condition likewise is secondary to bone infection. If the latter observation be a correct one the primary focus must necessarily be very mild, as a simple hydrops without other inflammatory signs is the only manifestation. Veeder and Jeans found 8 cases of simple effusion among 123 congenitally luetic children. There is no destruction of bone, and after treatment there is a complete restoration of the normal anatomical structures.

(*c*) *Arthropathie deformante syphilitique* is a type first described by Fournier. This interesting condition has been shown to be due to syphilitic changes occurring in the epiphyses, which give rise to osteophytic outgrowths resulting in ankylosis. As a general rule, the joint cavity is unaffected primarily and suffers only as its mobility is interfered with by the lipping of the bone. Clinically it is difficult to separate this type from a non-luetic chronic arthritis or arthritis deformans. Appearing insidiously in one or more joints it manifests itself by a slow but progressive stiffness and peri-articular swelling. The Roentgen-ray examination shows a smooth synovial surface, an intact cartilage, but a definite irregularity of the bone due to the above-mentioned osteophytic outgrowths. Such cases eventually have irremedial deformities much like our cases of arthritis deformans. Fraunthal believes that this group is pathognomonic of congenital lues, as distinguished from the synovial involvements which are common to many causes.

2. Arthropathies of Acquired Lues. The types of acquired syphilitic arthropathies vary in a measure with the stage of the

infection, although this rule is subject to many exceptions. Recent workers in syphilology have shown beyond question that one can no longer hold to the time-honored classifications of secondary and tertiary lesions. This is undoubtedly true of the almost whimsical manner in which the joints may be attacked. Neumann ventures the theory that in the early stages, while the spirochetes are still in the blood stream, the infection is more likely to be polyarticular. After the period of spirillemia has passed the organisms become localized in *loci resistentiæ minoris,* where later the process manifests itself. This is borne out largely by his clinical observations. To suit our present need, however, it will suffice to describe the different forms of joint lesion in acquired syphilis in their relations to the periods of the original infection.

I. ARTHROPATHIES OCCURRING EARLY. 1. In the early stage of acquired syphilis we commonly find an *arthralgia,* usually not associated with other local manifestations. It has no definite pathology, but according to Patton, Tubby, and others many of these painful joints develop a true serous synovitis, characterized by redness, swelling, and deep-seated pain. Curiously enough the pain is not, as a rule, increased by motion; in fact, it is frequently diminished. It is experienced by the great majority of syphilitics, and it occurs usually very early, sometimes preceding the skin rash. There is apparently no restriction of motion, but the pain may be intense, of a boring character, and mostly nocturnal. It is generally transitory, affecting many joints, and may be entirely absent during the day. Fournier has insisted that these arthralgias, so frequent in syphilis, are often due to involvement of the bursæ of tendons, for the reason that careful examination of the site of the pain, of the movements which elicit it, and of the directions along which it is transmitted often establishes its independence of the joints and points to its seat in the tendons.

2. Another type very common to this stage is an *acute or subacute synovitis.* It may replace the arthralgia or may occur quite independently of it. There is no evidence of an epiphyseal or bone involvement, so we may consider it a direct hematogenous joint infection. Its onset is often sudden, and may not be accompanied by any other signs or symptoms. Pain is generally present, but it is not, as a rule, exaggerated by movement; there is usually no constitutional disturbance, but, according to O'Reilly, the synovitis may be preceded by considerable malaise. However, in some cases the process may be sufficiently extensive and severe to simulate acute rheumatic fever. The previous history, the frequent association of cardiac complications, the acid sweats, etc., of the latter disease usually suffice for differentiation.

Waterhouse reports a case of a young man who at the disappearance of his specific skin rash was suddenly taken with pain and swelling in his right shoulder, later involving his left knee and right foot. His tonsils were inflamed and mucous patches covered his anterior pillars. There was general glandular enlargement and a temperature of 100°. Levine and Goldthwaite believe that the condition may simulate gonorrheal arthritis. Whitman says that the knees, shoulders, elbow, and sternoclavicular joints are most often involved. These patients are not relieved of their pain by salicylates. Lancereaux reports one case of acute synovitis in the ankles and knees in which 160 grains of salicylic acid were used daily for one week without effect, but there was prompt relief after the administration of mercury and iodides.

3. Another type, occurring usually as a late secondary manifestation, is a *hydrarthrosis*. It is generally slow in its onset, unassociated with other signs, and practically always affects the knee. This hydrops is usually painless and may similate a tuberculous joint. There is no bone destruction, and the mobility of the joint is not impaired. It runs a very chronic course and, according to Patton, may succeed the more acute synovial effusion. It is not at all characteristic of syphilis, and its recognition depends largely upon other associated data.

4. At about this period, or during later stages of a syphilitic infection, there is sometimes found an unusual picture very closely similating an arthritis. I refer to *infections of the bursæ*, and I include them in this review of arthropathies because of the intimate anatomical relationship as well as the clinical aspects of the two structures. We are indebted to Verneuil, in 1868, for the first description of this interesting condition. Since then other writers have recognized the luetic bursopathy of Verneuil, and have pointed out its similarity to arthritis. The chief bursæ in connection with syphilitic infections are those at the elbow, the wrist, the knee, and the ankle. Of these several joints the region of the knee is more richly supplied with bursal structures, and deserves special mention. According to Poirier, there are six bursæ lying in close proximity to the patella. The largest one is at the medial region of the knee, and is probably more frequently involved than the others. Curiously enough, only 26 cases have been reported, and of these, 9 occurred in the secondary and 17 in the tertiary period. Rather than consider this a true index of its infrequency, it is more probable that such pseudo-arthropathies have not been accurately differentiated from other articular or periarticular conditions. The most exhaustive description is given by Churchman, from whom I quote: "The picture, then, is one of an indolent affection of the bursæ, involving most often the knees, particularly in women. The disease is quite independent of syphilitic arthritis, the bursæ involved being oftenest those unconnected with the joints, and the neighboring joints being themselves entirely free from involvement. In the secondary stage, gummatous ulcerating and fungus forms occurs. The bursæ involved are those the most exposed to

trauma, but a study of the cases makes it clear that trauma, as usual in syphilis, only determines the site which the disease occupies. There is little or no accompanying functional disability. In view of the marked indolence of the condition and its great similarity to the arthropathies of syphilis, it should be spoken of as luetic bursopathy."

II. ARTHROPATHIES OCCURRING LATE. The joint affections occurring in the so-called tertiary period of lues form a chapter somewhat different from those noted in the earlier stages of the disease. This statement, however, is subject to notable exceptions, and one finds it difficult at times to determine the stage of the infection by the type of the joint process.

1. A gumma located in the peri-articular tissues may involve these structures and produce a picture resembling tuberculosis of the joint. This was originally described by Richet under the name of "tumeurs blanches syphilitiques." According to Levine, there is first thrown out an extracapsular edema which later results in a destruction of the bone and cartilage and gives rise to a chronic arthritis. Unless treatment is instituted early in such cases, ankylosis results. Bronchin, Richet, and Lancereaux report typical cases where the gumma had so completely filled the joint cavity as to be almost identical in appearance with an advanced tuberculous infection. There is usually considerable pain in these cases as well as effusion.

2. In another form the gumma may begin in the bone or cartilage and resemble an osteo-arthritis; the condition is known as *gummatous osteo-arthritis.* The Roentgen-ray plates show a loss of tissue in circular, pit-like excavations and not at points of greatest pressure, as in the non-specific arthritides. There is never any increase in cartilage to form ecchondroses, yet there is, as a rule, a proliferative periostitis (Patton). Clinically, these cases are of the arthritis deformans type, but, as a rule, they are not polyarticular. Waterhouse belives that osteoarthritis is prone to be found in joints which have been previously damaged by luetic infections. Other authorities feel that every patient presenting signs of arthritis deformans (except the senile type) should have a Wassermann test made, as it is otherwise impossible to differentiate the specific from the non-specific forms. Skillern emphasizes trauma as an allied factor in producing a deforming arthritis of this type. Suffice it to say, experience has shown that syphilis is capable of producing such a condition; while it is infrequent, the possibility of its occurrence should not be lost sight of.

3. Just as we may find a simple *synovitis* in the earlier stages, it sometimes appears also in the tertiary period. Generally the knee is involved. The condition is characterized by a more or less painful effusion into the joints. There is considerable stiffness and often creaking. On examination, aside from effusion, there is

definite thickening of the capsule and occasionally a slight elevation of local temperature. Whereas most of these cases run a chronic course, some of them are characterized by acute invasion, and the condition may resemble rheumatic fever. The effusion is often intermittent, and may recur without warning over night. Certainly, we are justified in strongly suspecting syphilis whenever there is a sudden appearance of synovial fluid without a history of recent trauma.

4. A review of this subject would not be complete without a reference to a type which is found in the late stage of syphilis, and which, since it was first described by Charcot, is known as Charcot's joint. Occurring especially in tabes dorsalis it is probably the best known of all the arthropathies associated with syphilis. The knee-joint is most frequently affected; next in frequency come the hip- and shoulder-joint, but marked and similar trophic changes also occur in the elbows and in the finger-joints. As is well known, the chief characteristic is an enormous, sudden, swelling about the joint, with little or no increase of synovial fluid. The joint is much enlarged, remains normal in color, and is absolutely painless. These arthropathies may appear early, and if they become chronic may lead to grotesque deformities; the bones become porous, giving rise frequently to fractures in, and about the joints. According to Peterson they occur in 3 to 4 per cent. of all tabetics.

Accepting the above types as representatives of the various joint lesions found in syphilis, we may tabulate them under the following headings:

Congenital syphilitic lesions	Osteochronditis syphilitica. Simple synovial effusion. Arthropathic deformante.
Secondary syphilitic lesions	Arthralgia. Acute synovitis. Hydrarthrosis. Bursopathy of Verneuil.
Late syphilitic lesions . .	Bursopathy of Verneuil. Tumeurs blanches syphilitiques. Acute or chronic synovitis. Gummatous osteo-arthritis. Charcot's joint.

The first of the two cases reported in the present paper is particularly interesting in that it so closely simulated acute rheumatic fever in its history, mode of onset, and general symptomatology. It is all the more remarkable in that it occurred during the tertiary period of the man's luetic infection and at a time when the acute varieties are very uncommon. When an acute synovitis does make its appearance several years after the initial lesion it attacks generally only one joint according to numerous observations. The interest in the second case centres in the polyarticular involvement. It is difficult to conceive of these multiple foci harboring spirochetes for a number of years, yet if we accept the belief that these organisms become localized at the end of the secondary period and there await an excitant, such as trauma, to begin a reaction we must look further for the stimulating factors. When only one joint is involved the difficulty is not so great. Granting that such localizations take place during the earlier stages, is it possible that it will be eventually shown that syphilis sets up a reaction only in those organs or parts where some other noxa is, or has been, at work? The unknown noxa could be of chemical, of cellular, or of bacterial origin. It is a significant fact that practically every patient who suffers from syphilis of the liver is, or has been, an alcoholic. The studies of Opie, Whipple, and others on experimental cirrhosis of the liver have demonstrated that neither bacteria nor certain chemicals alone produce the lesions, but only when both are jointly at work can hepatic cirrhosis be established.

Obviously our main diagnostic responsibility consists in the recognition of these types by separating them from the great class of non-specific joint affections. This only can be done by painstaking observation and by the more frequent application of the Wassermann test to arthropathic cases. It is interesting to know that in at least one large hospital in the East a Wassermann test is made on every joint case regardless of its character. Syphilis of the liver was formerly a curiosity, yet we now keep it in mind as a possibility in the study of practically every hepatic case. Certainly the joints, since they are so readily exposed to trauma and are so prone to harbor infection, should not be neglected when we are searching for spirochetal abodes.

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REVIEWS

Principles of Bacteriology. A Practical Manual for Students and Physicians. By A. C. Abbott, M.D., Professor of Hygiene and Bacteriology and Director of the Laboratory of Hygiene, University of Pennsylvania. Pp. 650; 113 illustrations, 28 in colors. Philadelphia and New York: Lea & Febiger, 1915.

This new ninth edition of Abbott's *Bacteriology* deserves all the favorable criticisms that have been made of its earlier editions. It has long been the classic text-book on bacteriology in the English language for the beginner, and this edition brings its contents fully abreast of the times. The section upon the physiological functions of bacteria has been enlarged. There has been added new matter upon hemolysis, complement-fixation, and the Erhlich conception of the immunity reactions. Colored diagrams accompany the description of Erhlich's theory of immunity and are very helpful. To allow for this new material there has been some reduction in matter that was of only historical importance.

Dr. Abbott has the happy faculty in writing, as he has in talking, of presenting the details of technique, even the details of laboratory equipment and the use of apparatus, in such a concise and brief way as to make them attractive and easily remembered. This book is fully entitled to the flattering reception which has been accorded each new addition. T. G. M.

Therapeutics of the Circulation. By Sir Lauder Brunton, Bart., M.D., Sc.D., LL.D. (Aberd.), F.R.C.P., F.R.S.; Consulting Physician to St. Bartholomew's Hospital. Pp. 536; 3 illustrations. New York: Paul B. Hoeber.

This book is the fruit of a long and rich experience, both clinical and research, in the field of cardiovascular conditions. In its first edition it consisted of eight lectures delivered at the University of London in 1905, and as such was made to conform to certain experiments of the author which he had been asked to present. In this second edition he has enlarged the scope of the subject, has gone more into the work of other experimenters, and has made the sequence of the subjects more orderly. It is intended only as a supplement to other works on the circulation, and does not therefore go into all the aspects of cardiovascular conditions as is done in the usual text-book. It is primarily a treatise upon therapeutics, yet fifteen of the nineteen chapters are devoted to a discussion of physiology, pharmacology, and living pathology. This, however, serves to present a rational basis for the author's discussion of therapeutics, and is perhaps justifiable. The treatment, while not exhaustive, is up-to-date, and no symptom or sign of cardiovascular disease is left without some therapeutic suggestion. The author's style is clear, and he has the faculty of stating things in such a simple and brief way as to make them readily appreciated. His similies are numerous and quite effective. On the whole the book is readable and instructive. T. G. M.

Curschmann's Text-book on Nervous Diseases. By G. Aschaffenburg, Cologne; H. Curschmann, Mayence; R. Finkelnburg, Bonn; R. Gaupp, Tübingen; C. Hirsch, Göttingen; Fr. Jamin, Erlangen; J. Ibrahim, Munich; Fedor Krause, Berlin; M. Lewandowsky, Berlin; H. Liepmann, Berlin; L. R. Müller, Ausbgurg; H. Schlesinger, Vienna; S. Schoenborn, Heidelberg; H. Starck, Karlsruhe; H. Steinert, Leipsic. English Edition by Charles W. Burr, M.D. Pp. 552; 156 illustrations. Philadelphia: P. Blakiston's Son & Co., 1915.

It was a happy thought which was responsible for the translation of this *Text-book on Nervous Diseases*, edited by the well-known German neurologist H. Curschmann. This work, which is in two volumes, was published some years ago. The different parts of the book were written by well-known German neurologists selected especially for their capabilities in certain lines, and, as a consequence, the German edition is one of the best of the composite text-books, for the German editor did his work well and the various authors succeeded not only in fitting in with the whole scheme of the book, but also in writing monographs on the particular subjects selected for them.

The English edition, undertaken by Charles W. Burr, gives to American readers a splendid text-book on nervous diseases. In addition to this, the editor has also written a chapter on functional disorders, which is a complement to a previous chapter on this subject by another author. As can be readily understood, it would be most difficult to write an adequate review on a book of this sort, for to do so it would be necessary to criticise the work of many authors, which would be impossible in the space available.

Suffice it to say that in the American translation nothing has been lost. However, there is one pertinent criticism which can be made of this work, which of course is not the fault of the American translation or of its American editor. These volumes were written a number of years ago, before the very marked increase in our knowledge of syphilis of the nervous system, the Wassermann reaction, the various serological studies and treatment, and, as a consequence, the chapters on tabes, paresis, syphilis of the spinal cord and of the brain leave much to be desired. There are very few comments made upon the Wassermann reaction, practically none upon spinal fluid findings, and the modern treatment by salvarsan is altogether neglected.

T. H. W.

THE CANCER PROBLEM. By WILLIAM LEAMAN BAINBRIDGE, A.M., Sc.D., M.D., Professor of Surgery, New York Polyclinic Medical School and Hospital; Surgeon and Secretary of Committee of Scientific Research, New York Skin and Cancer Hospital; Honorary President, First International Congress for the Study of Tumors and Cancers, Heidelberg, 1906. Pp. 534; 38 plates, 14 maps, charts and diagrams. New York: Macmillan Company.

THIS presentation of the cancer problem attempts to summarize with considerable detail the results of the studies—statistical, experimental, histological, and clinical—hitherto made upon malignant disease. The author's task is rendered intensely difficult owing to the fragmentary character of our knowledge thus far and the impossibility of determining at this time the relative importance of the various more or less isolated facts at hand regarding neoplasms and their behavior. The various theories of cancer are presented, but we have as yet no satisfactory grounds upon which to select or discard from among them. The importance of greater attention to the collection of fuller and more accurate statistics concerning cancer is pointed out. The histopathology of neoplasms is treated in an extremely brief and general manner, with no attempt to describe in detail the types of neoplasms, although a few excellent plates of typical malignant neoplasms are introduced.

A section is devoted to methods of diagnosis, including a description of several of the methods of serodiagnosis that, as the author notes, have as yet proved of little or no value.

The importance of chronic inflammation and irritation in predisposing to cancer and an enumeration of the benign lesions likely to undergo malignant degeneration occupy a few pages. A variety of the cancer cures that have been put forward, but on investigation have proved worthless, are described, together with an outline of a method of testing the value of a cancer cure. The place of light, Roentgen-rays, radium, electricity, and other forms of physical therapy is discussed, and the conclusion reached that for superficial growths, or as an adjuvant to surgical measures, certain at least of them are of distinct value. The use of escharotics is condemned. A plea is made for greater efforts toward alleviating, especially by surgical methods, the sufferings of "inoperable" cases.

Finally, the importance of education, first of the medical profession and then of the laity, concerning cancer, is discussed, and the facts that we may wisely at this time bring before the laity are considered.

A classified bibliography of selected references concerning different phases of the cancer problem, and especially of articles giving further bibliographies, is appended.

Because of the as yet embryonic state of cancer research, this work is of value chiefly as a book of reference and as a portrayal of the variety of lines along which this problem is now being attacked.

J. H. A.

NERVOUS AND MENTAL DISEASES. By ARCHIBALD CHURCH, M.D., and FREDERICK PETERSON, M.D., Eighth edition. Pp. 940; 350 illustrations. Philadelphia and London: W. B. Saunders Company.

IT seems hardly necessary to review the eighth edition of any book, for the mere fact that repeated editions have been issued is the best indication of its merit. This work has been adopted by most medical schools, and is used by a great many physicians. One reason for its popularity is that it contains both a nervous and a mental section, practically two books in one, something which no other single volume has. Written as it is by two of the best-known medical teachers in this country, there should be no doubt as to its value.

Considerable new material has been added to this edition. It is interesting to note that in the neurological section, Baranyi's recent work has received consideration. Such subjects as infantile paralysis syphilis of the nervous system, and the study of the cerebrospinal fluid have been in large part rewritten. Not much attention is paid to psychanalysis either in the nervous or the mental parts of the work. This is a mistake, for although one may not believe in a subject, a text-book should contain at least a brief working outline of a method which is now being followed by a large number of physicians in this country. Practically no changes have been made in the mental section.

T. H. W.

FEVER: ITS THERMOTAXIS AND METABOLISM. By ISAAC OTT, A.M., M.D., Professor of Physiology, Medico-Chirurgical College, Philadelphia, etc. Pp. 166; 14 illustrations. New York: Paul B. Hoeber.

As one begins to read this handy little book, he is led to believe that he is about to learn something of practical value in a subject that almost constantly engages his attention; but he is disappointed, as he proceeds, to find the book only a *résumé* of the subject from a strictly chemical and physiological point of view, emphasizing quite freely the researches of the author himself along this line. It purports to be three lectures delivered by the author to his sophomore classes in physiology, but it is difficult to understand how any second-year medical student could grasp the subject as here presented. He goes into great detail regarding the locations and functions of the various thermic centres in the brain and cord and the nerves connected with them. He gives much emphasis to Crile's theory of kinetic energy. Various types of calorimeters are described in placing before us the results of calorimetric experiments. In the latter part of the book metabolism is discussed in its relation to fever. To the physiologist this book will be of value, but for the internist it is somewhat disappointing. T. G. M.

HAND-BOOK OF OBSTETRICS. FOR STUDENTS AND JUNIOR PRACTITIONERS IN INDIA. By KEDARNATH DAS, M.D., Teacher of Midwifery, Campbell Medical School; Obstetrician and Gynecologist to the Campbell Hospital, Calcutta; Fellow, Member of the Faculty of Medicine, and Examiner in Midwifery, Calcutta University; Fellow of the Royal Society of Medicine. Pp. 612 and 376 illustrations. Calcutta: Butterworth & Co. (India), Ltd.

THE long experience of the author as an obstetrician in India has particularly fitted him to write a book dealing with obstetrics as modified by the racial and climatic conditions existing in that country. Following a brief introductory historical sketch the major headings, pregnancy, labor, the puerperium, and obstetric surgery are taken up in detail. The book is a thoroughly practical treatise on obstetrics and includes sections dealing with the tropical diseases and native conditions which often complicate obstetrics in India.

In the chapters on the physiology of pregnancy it is noted that the heat of the tropical climate produces some interesting variations in the metabolism of a pregnant woman. In the case of the

European women resident in India there is an excessive excretion of phosphates; while among the Bengalees there is found a markedly lower excretion of urea than in Europeans. Pelvimetry receives considerable attention. The racial and dietetic factors cause a certain amount of mal-development of the pelvis. Owing to the small stature of native women, the generally contracted pelvis is the abnormal pelvis most frequently encountered; rachitic pelves are rare, while the author records nine cases of osteomalacic pelves in his practice.

The various obstetrical operations are described in full, stress being laid upon those necessary to deal with the long-neglected cases, the result of native ignorance and prejudice against timely surgical interference. There are a large number of well-chosen illustrations. The final chapter on obstetric "hints" contains some especially pertinent advice.

The book is worthy of a place in the library of any one practising obstetrics in a tropical country. P. F. W.

ATEMKUREN MIT 574 REZEPTEN. VON DR. MED. HENRY HUGHES. Zweite stark vermehrte Auflage. Mit 18 Abbildungen im Text. Würzburg: Curt Kabitzsch.

THE act of breathing and its use as a therapeutic agent is here discussed in a thorough, concise, and clear manner. The author analyzes the different phases of the respiratory act, and describes their particular effect in various conditions. Each individual respiration he divides into five different stages: (1) equal respiration, *i. e.*, inspiration and expiration, are of the same intensity and duration; (2) intensified inspiration; (3) prolonged inspiration; (4) intensified expiration; (5) prolonged expiration. Each of these various types of breathing has its special indications, and is used accordingly. Further differentiations of breathing are also made, such as the patient's position or special kind of motion during the respiratory exercises and their indications explained. The author strongly emphasizes the importance of detailed prescriptions. He rightly says: "There is an enormous difference if I say, 'Take a few deep breaths several times each day,' or if I give the patient a written prescription like the following:

Bad Soden am Taunus, May 1, 1914.
℞ Costal Breathing.
Inspiration 3 seconds + Expiration 3 seconds
40 respirations
or 4 minutes
at 8, 10, 12, 4, 6, 8 o'clock.

The book bears throughout the mark of a scientist of high type and of a writer of quite an uncommon literary talent. We think, however, that the author might have explained a little more fully the physiological action of the different types of breathing.

The reading of this unique book has given us great pleasure and much valuable information, and we recommend it heartily to members of the medical profession, and particularly to those interested in the subject of physical therapy. J. B. N.

SPEZIELLE PATHOLOGIE UND THERAPIE INNERER KRANKHEITEN. Edited by FRIEDRICH KRAUS and THEODOR BRUGSCH. In 10 volumes. Berlin and Vienna: Urban & Schwarzenberg.

THE publication of this latest German "System" continues in the customary fragmentary fashion, without regard to continuity of subject or volume. The fortieth to forty-second "Lieferung" includes articles on plague, chlorea, and typhus, by Professor Zlatogoroff, of St. Petersburg, and one on malignant tumors, by Professor Werner, of Heidelberg. These will eventually occupy pages 599 to 578 of the first half of the second volume. Another section, the forty-third to forty-seventh "Lieferung," Volume V, pages 435 to 722, concerns the digestive tract. Functional stomach tests are discussed by Dr. Earnest Fuld, of Berlin; disturbances of secretion, by Professor Kuttner of Berlin. It is obviously inexpedient to attempt to give here any extensive analysis or criticism of a comprehensive work of this kind. One notices, however, as a chance observation, that no mention is made of the fractional method of removal of gastric contents. It is suggested, as of old, to remove the contents (at the height of digestion) one hour after the ingestion of an Ewald or Boas test meal. The usual preponderance of German references and neglect of foreign authorities is present. That the chapters under notice, however, have been written with the customary German thoroughness is evident after very few minutes' perusal. E. B. K.

THE DEAF: THEIR POSITION IN SOCIETY AND THE PROVISION FOR THEIR EDUCATION IN THE UNITED STATES. By HARRY BEST. Pp. 340. New York: Thomas Y. Crowell Company.

THE purpose of the book is two-fold; in Part I the deaf and their place in society is considered and in Part II what provisions should be made for their education is discussed.

The attitude of society in America toward the deaf is thoroughly gone into, together with the means of preventing acquired or congenital deafness. There is a wealth of statistics, some of value and some worthless in drawing conclusions concerning the increase or decrease of deafness. The book, however, is of more value to the social economist and statistician than to the physician.

The appendix, consisting of a list of homes and schools for the deaf in each state, should be indispensable to those interested in the education of the deaf and dumb. B. D. P.

MENTAL DEFICIENCY (AMENTIA). By A. F. TREDGOLD, Consulting Physician to the National Association for the Feeble-minded, and to the Littleton Home for Defective Children. Second edition. Pp. 491; 67 illustrations. New York: William Wood & Co.

THIS is the second edition, revised and enlarged, of Dr. Tredgold's book on *Mental Deficiency.* There is no doubt that it is the best practical small work on the subject. It is clearly written, the subject is well presented, and the reader who once starts will undoubtedly finish the book. T. H. W.

A TEXT-BOOK FOR MIDWIVES. By JOHN S. FAIRBAIRN, M.A., B.M., B.CH. (Oxon.), F.R.C.P. (Lond.), F.R.C.S. (Eng.). Obstetric Physician, with charge of Out-patients and in charge of Maternity Ward, St. Thomas' Hospital; Lecturer on Midwifery, St. Thomas' Hospital Medical School. Pp. 317; 104 illustrations, 5 in color and 3 plates. London: Henry Frowde and Hodder and Stoughton.

IF a book with the scope and character of the present one is offered for the edification of the English midwives it must be apparent that they occupy a higher plane in obstetric practice than the midwives of America. However, their needs and desires must be understood by one who has been associated with them for over twenty years as lecturer and examiner.

The author offers a well developed text-book on obstetrics with especial reference to the needs and limitations of the midwife. A logical arrangement of the subject is carried out which considers the science and art of obstetrics in all details. There are frequent explanatory notes in the text dealing with the rules of the Central Midwives Board, under whose supervision the practice of the midwives is carried on. The treatment of the most serious obstetric emergencies is fully described for those who under certain circumstances must assume the entire responsibility of such cases.

The last part of the book discusses venereal diseases, cancer of the womb, the midwife's duties, and the rules of the midwives' examining board; this latter section should prove valuable to those interested in the solution of this problem in America. An appendix, glossary and copious index complete the volume. The illustrations are well chosen.

While the book is above the understanding of the average foreign-born midwife of this country, it will be of assistance to those engaged in their training or regulation. P. F. W.

PSYCHOLOGY OF INTEMPERANCE. By G. E. PARTRIDGE, PH.D., Formerly Lecturer in Clark University. Pp. 275. New York: Sturgis & Walton Co.

THIS small book is a popular attempt to present the nature of intoxication and the craving for this and other stimulants. The author takes the viewpoint that to intelligently cope with the question of control of alcoholism we must first better understand the causes leading to alcoholism. He begins by a discussion of intoxication in animals, then among primitive and savage people and finally among civilized nations. He also discusses intoxication motives in literature, the mental and physical effects of intoxicants and the influence on abnormal cases.

In the second part the author takes up the practical problem of alcoholism, the saloon and the club, and preventative and educational measures. He does not believe much in the abolition of alcoholic habits by law but very sanely concludes that the cure of intemperance lies in the education of the young. T. H. W.

PRACTICAL GUIDE TO DISEASES OF THE NOSE, THROAT, AND EAR. By WM. LAMB, M.D., C.M. (Edin.), F.R.C.P. (Lond.), Honorary Surgeon Birmingham Ear and Throat Hospital. Third edition, 12 mo., 368 pages; 2 plates; 57 engravings. New York: William Wood & Co.

THE subject matter in this last edition has been revised and special sections added to parts of the second edition, notably the article on oral sepsis, a most important adjunct to throat conditions. The other additions embrance, the occasional risks attending the tonsil and adenoid operation, tonsillectomy and the submucous resection of the septum, danger signs in ear disease, the Heath mastoid operation and the examination of the labyrinth.

The entire book brings out the practical side of the subject and the mistakes one might make in diagnosis. The student wishing to perfect himself in theories must use some book of reference in conjunction with this practical manual. The last fifteen pages are devoted to formulas which have been tried and found of value in the author's own practice. B. D. P.

METHOD AND INDICATIONS FOR RADIATION WITH THE QUARTZ LAMP (ANLEITUNG UND INDIKATIONEN F. BESTRAHLUNGEN MIT DER QUARZLAMPE—"KÜNSTLICHE HÖHENSONNE"). By DR. HUGO BACH, Bad Elster i. Sachsen. Pp. 43; 5 illustrations and 1 color plate. Würzburg: Curt Kabitzsch, 1915.

THE author of this pamphlet exploits a new model ultra-violet lamp which seems to be constructed somewhat upon the principles of the well-known Cooper-Hewitt lamp, with the important modification that the tube is composed of quartz instead of glass, thus permitting the escape of a much larger percentage of ultra-violet rays. The lamp, its mechanism and the technic of its use are fully described. The author sets forth a large number of superficial, general and organic conditions in which the light may be used and in which it has been employed by himself and others with more or less success. H. K. P.

THERAPEUTICS OF DRY HOT AIR. By CLARENCE EDWARD SKINNER, M.D., LL.D. Third edition. Pp. 336. Hammond, Indiana: Frank S. Betz Company.

THE book is divided into thirteen chapters. The first of these gives a description of the apparatus, the second deals with the physiological action, and the third with the technique of dry hot air treatment. In Chapters IV to XI the nature and treatment of various diseases are discussed. In addition to the dry hot air treatment other remedial measures which may be of advantage in conjunction with dry hot air are briefly mentioned. Chapter XII is devoted to fields of future research and Chapter XIII to the incandescent electric light.

The author devotes little attention to the differentiation of active and passive hyperemia and of dry and moist heat, their different physiological properties, effects, and indications. Furthermore the temperature, duration, and frequency of the dry hot air applications as devised in this book are altogether too severe.

As to the effect of the treatment by dry hot air the book abounds in claims which appear to us to be decidedly overdrawn. To substantiate these claims the author frequently goes into lengthy arguments which, unfortunately, frequently show lack of sound reasoning.

We doubt whether the repeated reference in this book to the particular apparatus manufactured by a certain company is compatible with the best form of professional ethics. J. B. N.

The Early Diagnosis of Heart Failure and Other Essays on the Heart and Circulation. By T. Stacey Wilson, Senior Physician, General Hospital, Birmingham, etc. Pp. 617; 163 figures and 12 plates. New York: William Wood & Co., 1915.

The author states that his aim is to help the practitioner when at the bedside, by suggesting to him new methods of observations which give fresh insight into the mode of the heart's action in health and disease. A collection of seventeen essays written in a period of over twenty years, however, would seldom be considered the happiest medium for "advancing new theories, advocating new methods," even though as in the present instance, many of the facts are recapitulated in a sixty page summary. The author lays stress on the importance of the "distensibility" of the heart, but fails to convince that his simple methods of examination have demonstrated the changes he discusses. For instance, in speaking of the distensibility of the conus arteriosus being diminished as the fibrous strength of the heart and pericardium increases with advancing years, he says that rheumatic fever appears to increase distensibility by softening the fibrous element of the heart (?). We are willing to admit that "such conditions as 'high diaphragm' and 'diminution in the areas of the liver dulness' are rarely looked for as signs of diminution of the total volume of blood in circulation, nor is this lessened volume of circulating blood generally recognized as a sign of myocardial weakness," but before we are willing to accept such questionable hypotheses, much fuller and more accurate proof should be forthcoming than these essays afford. Scattered through the rambling subject matter, on the other hand, are numerous valuable clinical observations, such as those concerning the significance of different positions of the apex best, and at least one valuable improvement in method is suggested in an adaptation from Marey's and Galabin's cardiograph, which "records as many as sixteen to eighteen distinct waves associated with each cardiac cycle."

One is forced to the conclusion that whereas this book is both instructive and suggestive to the specializing student of cardiac pathology, it is emphatically not valuable for the general practitioner, and might even do him harm by clouding the proved cardiac theories now generally accepted. E. B. K.

Die Nebenwirkungen der Modernen Arzneimittel. By Professor Dr. Otto Seifert. Pp. 283. Würzburg: Curt Kabitzsch, 1915.

In the introduction to a previous publication by the author on this subject, he explains that his purpose is to give to the general practitioner a complete presentation of the more valuable modern remedies, with especial emphasis on the symptoms produced by toxic doses. To this end, over six hundred drugs, the majority of them quite unknown to the reviewer, have been arranged alphabetically in sixteen groups, such as antipyretics, whooping-cough drugs, antigonorrheics, etc. The name, composition, dosage and toxicology of each remedy is presented, and, still further to assist the general practitioner, an alphabetical list at the end includes the name of the manufacturer of each drug. To the busy practitioner with a penchant for giving the latest remedy, or with a clientele that demands the same, this book, if frequently supplemented, should be of value. He can in most cases find out more about the remedy in question that is told in its accompanying circular, whereas, if he relied on the list of remedies passed by the Council of Pharmacy, he would in most cases, not find the drug at all. E. B. K.

The Intervertebral Foramina in Man. By Harold Swanberg, Member of American Association for Advancement of Science. Pp. 95; 11 original full-page plates. Chicago: Chicago Scientific Publishing Company, 1915.

Swanberg presents a second brief outline of the intervertebral structures dealing exclusively with the intervertebral foramina in man. He has described the variation of the intervertebral foramina at different levels and the structures which pass through them. This study of these foramina emphasizes the importance of a thorough knowledge of the anatomical relationships when pathological conditions are under consideration. This small book, as a supplement to his first book, is of value both to the surgeon and to the physician. W. J. M.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF
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AND

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Magnesium Glycerophosphate in Place of the Sulphate in the Treatment of Tetanus.—ZUELZER (*Berl. klin. Wchnschr.*, 1915, lii, 689) states that magnesium glycerophosphate is as effectual as magnesium sulphate in the treatment of tetanus with decidedly less toxic action. He ascribes this partly to the fact that glycerophosphoric acid is a cleavage product of lecithin and hence less toxic to nerve tissue. Zuelzer found that the severest symptoms subsided promptly under its use. He gave it in doses of 10 c.c. of a 25 per cent. solution every three or four hours to moderately severe cases. This dosage controlled convulsions and the patients were kept almost entirely free from pain. This treatment can be continued for days without any untoward symptoms. No appreciable effect upon the pulse was observed under continued treatment. Animal experiments showed that the glycerophosphate produced a much less marked fall in blood-pressure as compared with the sulphate.

Extirpation of the Pineal Body.—DANDY (*Jour. Exper. Med.*, 1915, xxii, 237) publishes his observations on dogs after complete extirpation of the pineal gland. In view of the recent marked advances in our knowledge due to a thorough study of the other glands of internal secretion, it was natural to expect that some such powerful influence on the body might result from the internal secretion of this gland. The basis for this assumption is chiefly due to clinical observations on cases dying of tumors of this structure. The experimental data have so far led to very inconclusive results. In the work here reported, the complete removal of the gland has been accomplished by a comparatively simple operation and with almost completely negative results.

The author's conclusions are as follows: (1) "Following the removal of the pineal, I have observed no sexual precocity or indolence; no adiposity or emaciation; no somatic or mental precocity or retardation. (2) Our experiments seem to have yielded nothing to sustain the view that the pineal gland has an active endocrine function of importance either in the very young or adult dogs. (3) The pineal is apparently not essential to life and seems to have no influence upon the animal's well being."

Bacteriotherapy in Typhoid Fever.—JOBLING and PETERSON (*Jour. Amer. Med. Assn.*, 1915, lxv, 515) note that during the past few months there have been published a number of interesting observations dealing with the bacteriotherapy of typhoid fever, largely the result of experience gained by using sanitarians in the eastern front of the European war. The most encouraging reports have dealt with the therapeutic use of intravenous injections of sensitized vaccine. The dosage used has varied considerably, from the minimum of about 50 million to a maximum of 800 million. Ischa Rawa considers the mortality reduced by one-half and practically all the case reports recently published have shown similar results. However, isolated cases have been reported in which the injection of the vaccine was followed by alarming collapse symptoms. These reports emphasize more especially the increase in peristalsis with consequent danger of hemorrhage and perforation and the cardiac collapse that may result. Even subcutaneous inoculations of immunizing doses are known to stimulate the intestinal tract. In view of certain definite objections to the vaccine treatment with typhoid bacteria, such as the increase in peristalsis and the deleterious effect on the heart, the authors think it rational to endeavor to obtain the stimulation of the ferments by some means other than one involving the danger of further injury to the patient. Such a method might be found by using the various split products of the bacterium or other proteins and avoiding those which are known to be the most toxic. As Zung, and Jobling and Strause have shown, the protoalbumose fraction of the protein split products is usually very toxic, while the secondary proteoses are practically non-poisonous. Lüdke has already made some applications of such treatment and has reported very favorable results. A series of cases which the authors have under treatment at present, while not sufficiently large to permit definite conclusions, seems to afford a very favorable confirmation of Lüdke's results. They believe that the conclusion is warranted at present that intravenous bacteriotherapy offers a reasonably safe method of treatment in select cases of typhoid fever, but that further efforts should be made to overcome the definite toxic effects which of necessity accompany the injections. In the mechanism of the reaction the authors are of the opinion that the non-specific ferments are of considerable importance.

Results Obtained from the Induced Pneumothorax Treatment of Pulmonary Tuberculosis.—SLOAN (*Johns Hopkins Hosp. Bull.*, 1915, xxvi, 289) presents a brief report regarding results obtained in the treatment of pulmonary tuberculosis by artificial pneumothorax. He includes in this article 20 cases previously reported by Hammon and himself and adds 23 cases to this series. The author selects as suitable for this method of treatment patients showing: (*a*) gross and active lesions in one lung with a quiescent lesion not extending below the level of the fourth rib in the other lung; (*b*) gross and active lesions in one lung, with a mildly active lesion not extending below the level of the third rib in the other; (*c*) quiescent lesions, bilateral but suitably located, with a history of aggravating cough and profuse expectoration; (*d*) arrested but suitably located lesions, with a previous history of relapse whenever work was attempted; (*e*) arrested lesions, but with a history of recurring hemorrhages. Patients with incipient lesions have been considered unsuitable, except in cases of hemorrhage. All of the patients treated had moderately or far advanced pulmonary tuberculosis, except one, who had bronchiectasis. Those designated as unsuitable were patients showing: (*a*) gross and active lesions extending below the level of the third rib on both sides; (*b*) an extensive gross lesion in one lung and a lesion located at the base in the other; (*c*) serious complications such as cardiac disease, arteriosclerosis, ulcerative laryngitis, chronic diarrhea, extensive tuberculous ostitis and nephritis, either acute or chronic; (*d*) disease apparently of long standing, as shown by marked fibrosis of the lungs, thoracic deformities, decided cardiac displacement and dyspnea; (*e*) a history of chronic alcoholism; (*f*) a history of recurring hemorrhages from both lungs; (*g*) a marked emphysema; (*h*) an erratic or excitable temperament; (*i*) real or apparent old age. Of the 43 cases treated no collapse of lung was produced in five cases, and only a partial collapse was obtained in 15 cases. Those in whom only a partial collapse was produced seemed to experience as much symptomatic relief as those in whom a complete collapse was obtained. Of the 43 patients who were treated from three months to three and a half years, 18 or 41+ per cent. have died, and 25 or 58+ per cent. are living. Of these 25 living, 8 or 19+ per cent. of the whole, are doing poorly; 11 or 26+ per cent. are doing well and are working part time. Six, or 14+ per cent. have resumed all of their former business and social obligations. Sloan in conclusion states that the induced pneumothorax treatment applied to the 42 patients with moderately or far-advanced pulmonary tuberculosis and one with bronchiectasis, influenced the progressing course of the disease little or none at all in 60 per cent. It did, however, stop distressing symptoms in a large number of this group. In addition the author believes that the fact that this treatment restored 11 per cent. of the patients to perfect health and complete working capacity for over two and a half years justifies the use of the method.

Typhoid Fever in the Vaccinated.—BOURGES (*Bull. de l'Acad. de Méd.*, 1915, lxxiii, 785) says that among 550 typhoid patients at Brest in the last two years, fifty-three had received protective inoculation against typhoid fever. In this vaccinated group the disease was of mild or average type in all but five where it was of the severe type and proved fatal to all. One of these patients had only received one injection of the vaccine and should be excluded as not completely vaccinated. Excluding two others of this group who died chiefly as a result of secondary infection, there remains only two fatalities to be ascribed directly to the typhoid. This mortality compares very favorably to a mortality of 15.2 per cent. occurring among those not receiving the prophylactic treatment.

SURGERY

UNDER THE CHARGE OF

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AND

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The Employment of the Tuberosity of the Os Calcis and the Patella for the Secondary Covering of a Stump after Amputation for Suppuration.—Oehlerecker (*Zentralbl. f. Chir.*, 1915, xlii, 473) calls attention to a method of later improving the bone end left by the removal of the lower third of the leg or thigh, when the wound has been left open for drainage on account of the presence of severe infection, at the time of the amputation. The principle in such an operation is the same as that of the Pirigoff and Gritti amputations. Three or four months after the amputation, when the infection has been overcome, the wound surface has become clean and the flap containing the tuberosity of the os calcis or the patella has contracted, a secondary bony union is obtained and the diaphyseal end of the diaphysis covered by an osteoplastic flap. Two war cases are reported. In one the ankle joint was severely infected, the astragalus necrotic and the soft tissues of the lower part of the leg and foot was the seat of a phlegmonous inflammation. A posterior flap was made including a part of the tuberosity of the os calcis, the bones were divided at about the junction of the lower and middle thirds of the leg and the wound left open until clean, about four months later, when it was much smaller. The bone ends were freshened by a sharp curette and approximated, the heel flap being held in position by strips of adhesive plaster. Firm and rapid union resulted and the patient was discharged with an artificial leg, the stump taking the weight in an excellent manner without pain. The same result was obtained after an amputation through the lower end of the femur with an anterior flap containing the patella, the patella being approximated to the lower end of the femur about three months after the amputation and an excellent weight-bearing stump being obtained.

Fulguration in the Treatment of Tumors of the Bladder.—Geraghty (*Surg., Gynec. and Obst.*, 1915, xxi, 150) says that only in papillomata has fulguration been destructive, and it has destroyed the malignant as well as the benign papillomata. Where the tumors are cystoscopically and histologically benign the rapidity of disappearance is frequently astonishing. When they are malignant, the response may be extremely slow and lead almost to discouragement. Where they are distinctly malignant, the response is almost certain to be slow. Sometimes small malignant papillomata will require many times the amount of treatment which would have been necessary for a benign papilloma of the same size. In one case with multiple malignant papillomata covering the left lateral wall of the bladder and the tumors so fused at their surfaces that it seemed like one large tumor mass, seventy-five treatments, extending over a period of nine months, were necessary to entirely eradicate the neoplasms. No radical operation could have given as complete a result. In the papillary carcinoma or sessile tumors, where infiltration of the base is always present, the chances of eradication of the tumor by this method of treatment are practically *nil*, although considerable symptomatic relief may at times be obtained. From the standpoint of ultimate prognosis it is important to have a knowledge of the nature of the growth removed, because in three of his cases in which malignant papilloma had been successfully removed, death occurred later from metastases, although the bladder remained free of tumor. Furthermore, recurrences have been encountered only in cases in which malignant papilloma had been removed. It can now be positively stated that fulguration should be the treatment selected for all papillomata, benign or malignant, in which infiltration of the bladder wall has not occurred, and that it yields results incomparably superior to the most radical operative procedures.

The Desiccation Treatment of Bladder Tumors.—KEYES (*Surg., Gynec. and Obst.*, 1915, xxi, 169) applied the desiccation treatment (fulguration) to 27 personal cases and by adding those cases communicated to him by nine other surgeons, he was able to report 126 cases. Tumors of the bladder must be classified as benign or malignant in accordance with their clinical characteristics, especially their reaction to the desiccation treatment. The clinical characteristics of malignancy are hardness of the tumor, intractable cystitis, and sloughing or ulceration of the tumor. Multiplicity and size of the tumor militate against the success of any treatment. The surgeon will have to decide from his own experience which cases are to be selected for desiccation, and which submitted to operation and desiccation afterward. When a bladder contains more than two or three tumors we may prophecy a continual tendency to relapse, and we must insist upon the closest vigilance after apparent cure. For two weeks after each treatment the patient should be within call of the physician qualified to care for either infection or hemorrhage. Cures should be verified as follows: Cystoscopy must show the bladder entirely healed. Three months later cystoscopy must be repeated. One year after this it must be repeated again. Further cystoscopic verification must be made at periods of about three years. For how long the tendency to relapse continues, we do not know; but after the first year it is probably slight. Death has resulted once from hemorrhage and twice from "pericystitis."

The Pathological Diagnosis of Tumors of the Bladder with Particular Reference to Papilloma and Carcinoma.—BUERGER (*Surg., Gynec. and Obst.*, 1915, xxi, 179) says that from a study of one hundred and thirteen tumors of the bladder, amongst which there were fifty-five papillomata, forty-five papillary carcinomata, five squamous carcinomata, two metastatic carcinomata, and six sarcomata, he was able to conclude that a differential diagnosis between the papillomata and carcinomata can be made in almost all instances on a pathological basis. Certain morphological criteria were accepted as indicating the existence or the acquisition of malignant traits in any given tumor. These criteria were found to be present in parts of the tumor that are accessible in so far as they can be reached by cystoscopic instruments, and in so far as adequate portions can be removed for histological examination. The changes that are indicative of malignancy occur, not as heretofore assumed, in the "depth" where they may escape our diagnostic methods, but manifest themselves first, in the epithelium, not far from the surface, either with or without areas of infiltration. A test of the morphological criteria proved conclusively that they are dependable and, if adopted, lead to correct diagnosis. Many of the other loosely accepted notions regarding the malignancy of papillomata *per se* were found to be fallacious. Only in one tumor out of one hundred and thirteen was a papilloma found to infiltrate and still retain "normal" cellular characteristics.

Frequency of Recurrence of Stone in the Kidney after Operation.—CABOT and CRABTREE (*Surg., Gynec. and Obst.*, 1915, xxi, 223) say it has been clearly shown that the risk of these operations is not great. In their series of 155 cases there were 5 deaths, 2 following nephrectomy, and 1 each following nephrotomy, pyelotomy and ureterotomy. On the basis of these cases they can only say to the patient that the risk of operation is small; that the danger of progressive destruction of the kidney by the stone, if it is left, is large; that the probability of recurrence is considerable; that it depends somewhat upon the age, undoubtedly somewhat upon the method of operation and the skill with which it is carried out, but clearly somewhat upon the entirely unknown factor—the liability or the ability of that particular kidney to form concretions. The outlook for the cases of stone in the ureter is apparently considerably better. In this small series of 21 cases, the probability of permanent cure seems to be about two to one.

Note on the Anatomy of Imperfectly Descended Testes.—WOOD (*Surg., Gynec. and Obst.*, 1915, xxi, 232) has had the opportunity of dissecting six specimens of undescended testes. Among other findings in five of the six specimens the vas deferens was found to terminate in a series of coils with a blind extremity which was not attached to the testis in any way. These coils appear to represent the globus minor of the epididymis. He presents a study of the subject and emphasizes that failure in the descent of the testis is due to developmental defects that take place very early in fetal life. The degree of the abnormality corresponds to the extent of interference in the formative period. As is well known, prior to the fifth or sixth week the sex characteristic can not be distinguished. It has seemed to Wood that, in the condition here alluded to, the impress of the stimulus that determines the sex has been deficient, so that the change from the primary indifferent stage has stopped short of perfection. As a consequence there are definite anatomical defects observed in connection with the testis which may involve other structures derived from the same embryological source. As the majority of detained testes reach the scrotum by the time of puberty, in the absence of complications that demand relief it would seem wise to postpone operation for transplanting the testis in the scrotum until ample time has been given the organ to descend naturally. When operation is undertaken for any reason a effort should be made to trace the vas, and if it is found not to be connected with the testis an anastomosis may be performed, particularly if spermatozoa are present.

THERAPEUTICS

UNDER THE CHARGE OF

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Whooping Cough.—Luttinger (*New York Med. Jour.*, 1915, ci, 1043) reports 138 cases of whooping cough treated with stock vaccines prepared by the New York Health Department. Of this series of cases, 115 came under treatment within the first three weeks of the paroxysmal stage. According to Luttinger, the vaccine treatment seems to have decreased the paroxysmal stage by over two weeks when compared to cases in which drugs alone were used. What was more significant to the author, however, than the shortening of the duration of the paroxysmal stage, was the prompt amelioration of the severity of the paroxysms which followed the administration of the vaccine in nearly all cases. On the other hand, the cases treated with drugs, as a rule, showed first a decrease in the number and not in the severity of the individual paroxysms. Luttinger who states that the vaccine seemed to have a prophylactic value when given in sufficiently high dossage.

Progress in the Use of Standard Salvarsanized Serum Intraspinally.—Ogilvie (*Med. Record*, 1915, lxxxvii, 1062) in a former paper, described a method of preparing *in vitro* a salvarsanized serum of standard strength suitable for administration intraspinally in syphilitic disorders of the central nervous system and reported 15 cases which had been treated with the preparation. His present paper deals with the results of continued treatment of the same series of cases. Out of the 15 cases, 13 show a complete disappearance of all subjective manifestations, with improvement in the objective signs in one way or another, for an average period of one year, while one showed moderate improvement only, and one failed utterly to respond to treatment. Of the total number, 11 cases (6 tabes, 3 paresis, 1 syphilitic myelitis, 1 cerebrospinal syphilis) show spinal fluids negative to the Wassermann reaction in all titrations, with normal cell and globulin contents; 2 remain positive, and in 2. recent analyses could not be secured. Ten cases (4 tabes, 4 paresis, 1 syphilitic myelitis, 1 cerebrospinal syphilis) show negative Wassermann reaction in the blood; 3 remained positive, and in 2, recent analyses could not be secured. As to the value of the treatment when systematically and judiciously employed, further comment seems unnecessary to Ogilvie. To those familiar with the resistive and tenacious character of these diseases it will at once be evident, from a study of this and other reports, that the intraspinal method offers far more in the way of therapeutic possibilities than the use of mercury and salvarsan intravenously alone. That the latter are of the greatest importance is readily conceded, but laboratory evidences of syphilis in the spinal fluid are completely eradicated in but few cases treated without intraspinal medication. Ogilvie states that no matter how striking the clinical improvement may be the treatment has been inadequate unless this has been accomplished. He emphasizes that in neurological syphilis the field of greatest opportunity lies in instituting treatment in the predestructive stage. With this end in view the spinal fluid should be subjected to a rigid examination in every case presenting indefinite or transitory symptoms referable to the central nervous system, whether the patient gives a history of syphilis or not and regardless of the existence of a negative Wassermann reaction in the blood.

Pollen Therapy in Hay Fever.—Goodale (*Boston Med. and Surg. Jour.*, 1915, clxxiii, 42) says that serobiological methods have shown the same phylogenetic relationship of the different plant orders and families. The application of these discoveries to the treatment of hay fever by injection of plant proteids promises to assist in the selection of the specific material for a given case. Definite reactions are elicited in hay fever by the pollen of the exciting plants, when brought into contact with an abrasion of the skin. The intensity of these skin manifestations may be easily diminished by the repeated parenteral administration of the proteids in question. Coincident with the diminution in the skin reactions, there seems to occur an increased tolerance of the exposed mucous membranes to the pollens of the plants employed. Pollen therapy in hay fever may be regarded at the present time as a promising method of treatment, but its value and the permanence of its results remain still to be definitely established.

The Intraspinal Administration of Antitoxin in Tetanus.—Nicoll (*Jour. Amer. Med. Assn.*, 1915, lxiv, 1982) says that the result of a series of animal experiments conducted by Park and himself was conclusive in showing that the intraspinal administration of tetanus antitoxin was far superior to the subcutaneous and intravenous methods of administration. As a result of this experimental work, the following method of treatment is strongly advised by Nicoll: (1) The intraspinal injection of from 3000 to 5000 units into the lumbar region of the spinal canal, preferably under an anesthetic, the volume of fluid injected being brought up to 10 or 15 c.c. by the addition of sterile normal saline, the exact amount being regulated according to the age of the patient and the amount of spinal fluid withdrawn. (2) The intravenous injection of 10,000 units at the same time. (3) The repetition of the intraspinal dose in twenty-four hours. (4) A subcutaneous injection of 10,000 units three or four days later. The well-recognized adjuvants to specific treatment (quiet, subdued light, sedatives, etc.) should be used to supplement the treatment as outlined. Nicoll reports 20 cases of tetanus treated on this plan and gives brief abstracts of the clinical histories of these cases. Of the 20 cases, 16 recovered. The author states that in judging the effect of antitoxin given intraspinally in this series of cases, it must be remembered that the cases were not selected, but that every case of tetanus reported was given the benefit of the treatment regardless of the clinical condition. The series, therefore, may be said to be fairly representative of the type of the disease occurring in and about the City of New York. A few of these patients would undoubtedly have recovered if the intraspinal injection of antitoxin had not been given or without any treatment other than symptomatic. The results obtained, however, in the saving of life are so much more favorable than those in previous years, when large doses of antitoxin were recommended to be given by the intravenous and subcutaneous methods, that there can be no reasonable doubt that the low death rate, 20 per cent., here obtained was largely due to intraspinal dosage.

Intraspinal Therapy in Syphilis of the Central Nervous System.—SWIFT (*Jour. Amer. Med. Assn.*, 1915, lxv, 209) believes that intraspinal injections of autosalvarsanized serum or serum to which a small amount of salvarsan or mercury is added, is of distinct help in certain cases of tabes and cerebrospinal syphilis. Not all patients with these diseases require intraspinal treatment. Many of them respond well to intravenous injections of salvarsan combined with mercury and iodide properly administered. In other cases, the symptoms and abnormal cerebrospinal fluid are not controlled by general therapy, and it is in this class that we believe the addition of intraspinal therapy to be of value. Both the clinical side and laboratory evidences of active disease should be considered, and any treatment controlled by repeated examinations of the blood and cerebrospinal fluid. Although the treatment of these diseases should be systematic, it should not be so rigid that individual indications should be disregarded. Not infrequently one sees improvement only after active treatment has been discontinued. Others seem to require constant treatment until all evidences of active disease have disappeared. Only by considering all the factors can consistent beneficial results be obtained.

The Starvation Method versus Gradual Carbohydrate Reduction as a Time Saver in the Treatment of Diabetes.—CHRISTIAN (*British Med. and Surg. Jour.*, 1915, clxxii, 929) says that the starvation method of Allen for rendering a diabetic sugar-free, in addition to being a safe method, has shortened very materially the time required to get a patient with diabetes sugar-free, and so permits of a large part of the patient's stay in the hospital being devoted to building up the patient's tolerance for carbohydrates. To put it another way, the method saves for the patient and for the hospital one or two weeks of time.

PEDIATRICS

UNDER THE CHARGE OF

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Etiological Relationship of Syphilis to Chorea of Sydenham.—Koplik (*Arch. Pediat.*, 1915, xxxii, 561) reports his investigation of cases of Sydenham's chorea with a view to proving an etiological relationship with syphilis. He avers the clinical connection between chorea and endocarditis and between chorea and rheumatic joint manifestations and states it as his belief that all chorea of the Sydenham type seems to be of an infectious nature. By investigating 11 cases of chorea he found no positive Wassermann reaction and no clinical or physical evidence of syphilis. By intravenous injection of salvarsan in 7 cases of chorea there was no especial improvement and certainly no "striking effect" has had been averred. He does not believe there is any connection between the two diseases and from the results of his investigation he concludes that salvarsan has no more value in chorea than what has hitherto been used in treating this disease.

Congenital Syphilis in Infants.—M. Soldin and F. Lesser (*Deutsch. med. Wchnschr.*, 1915, xli, 429) present the symptom-complex of a number of cases which have merely a suggestion of syphilitic disease and in which the Wassermann reaction was uniformly negative. The infants suffered primarily from nutritional disorders. Symptoms which suggested congenital syphilis in these cases were sniffling, discrete rose-colored macules on the soles of the feet showing no infiltration, post-cervical lymphatic enlargement only as large as rice kernels, and occasionally a slight and temporary enlargement of the liver and spleen. In every one of these cases the mother was found to have a positive Wassermann reaction and so turned a suspicion of the disease due to a faint symptom, to a conviction of the presence of a luetic taint. Toxic substances may have been transmitted to the child from its syphilitic mother sufficient to account for the suggestive symptom and yet the question may arise if the child be actually a spirochete carrier. Again all syphilitic symptoms of an active kind can be absent for many years and then suddenly develop. Systematic observation in families afflicted with congenital syphilis show that in one-half the cases congenital syphilis is latent during the early years. For practical purposes the authors lay down the rule, not to be content with a negative Wassermann reaction in an infant with suggestive luetic signs but to also examine the blood of its mother.

Treatment of Scarlet Fever.—R. Koch (*Deutsch. med. Wchnschr.*, 1915, xli, 372) compares the scarlet fever statistics of Barasch with his own and draws conclusions as to specific treatment in this disease. In ten years Barasch reports 1438 cases of scarlet fever with a mortality of

15 per cent., only 6.6 per cent. of deaths occurring after the third day. Koch reports 263 cases in one year with a total of three deaths, or 1.1 per cent. In Barasch's cases no specific treatment was carried to a definite conclusion, the treatment being general. In Koch's cases 28 of the most severe cases were treated by intravenous injection of "convalescent serum," taken from patients convalescent from scarlet fever. Of the 28 cases but 1 died. Of 12 cases, not quite as severe which were treated with normal human serum, 1 died. Koch remarks the difference in the two mortality records and implies that the small percentage in his cases is due to the employment of the serum. In Barasch's cases 122 out of 217 cases died during the first three days through general intoxication. It is in the very grave cases that the "convalescent serum" has its greatest effect when given early and in sufficiently large doses, 50 c.c. for small children and 100 c.c. for older cases. The serum has little if any effect when used in cases with complications of scarlet fever. The serum should be gathered from a number of convalescent cases and mixed. It is sterilized and combined with 0.5 per cent of a 4 per cent. carbolic acid solution.

Localizing Brain Symptoms as Early Events in Tuberculous Meningitis.—C. O. Hawthorne (*British Jour. Child. Dis.*, 1915, xii, 232) reports 2 cases of tuberculous meningitis which began during apparent good health with motor phenomena suggestive of a localized cerebral lesion. One child vomited and the following day was found to have a paralysis of the left face and left arm which cleared up in forty-eight hours, to be followed a day later by convulsive seizures of these parts, following which paralysis was again noted but other clinical signs absent, including the fundus of the eye and the spinal fluid. The paralysis disappeared entirely later on only to usher in the frank signs of a tuberculous meningitis. The other child was suddenly seized with right-sided convulsions which ceased in several hours and next day there were no clinical signs of disease to be found. Within three days convulsive seizures again appeared and he later developed a tubercular meningitis which was proven at autopsy. Convulsions and paresis usually come late in this disease and to explain the early symptoms mentioned in the above 2 cases, the author suggests that the sudden and limited motor phenomena marked the arrival of the specific irritant within the cranial cavity and its application to a localized area of brain tissue. Presumably, the effect of such emboli on the motor cortex would be capable of producing cortical disturbances which express themselves clinically either as unilateral paresis or unilateral convulsion followed after a time by local recovery of nerve function and still later by generalized signs of a meningitis from an extending infection. It does not seem possible to carry the position further than to say that at times the arrival of the infection in this disease may be marked by limited motor phenomena suggestive of a localized cerebral lesion.

Immunization against Measles.—C. Hermann (*Arch. Pediat.*, 1915, xxxii, 503) reports a series of tests in immunizing infants against measles. The basis for his idea is that infants under five months are relatively immune to measles or when they are infected the disease appears in a mild typical form. Under two months infants are absolutely immune. The immunity becomes less marked toward the end of tbe first year and during he second year is entirely absent. Infants under five months coming in intimate contact with measles without being infected frequently do not contract the disease when exposed later. One attack of measles usually protects for life. Also the immunity cannot be transferred by the mother solely through the breast milk for artificially fed infants are also immune. The infant possibly elaborates its own antibodies. Also the nasal discharge contains the virus twenty-four hours before the appearance of the eruption in measles. Based on these facts the theory is to inoculate infants under five months with measles virus, thereby conferring an immunity by manufacturing antibodies while the child is least susceptible or at most will take the disease in a mild atypical form. Up to this time 40 infants have been inoculated at the following ages: 1 at two and a half months; 4 at three months; 3 at three and a half months; 6 at four months; 15 at four and one half months, and 11 at five months. The majority of the infants showed no distinct reaction. Fifteen had a slight rise of temperature from the eighth to the fourteenth day and in a few instances a few indistinct spots were noticed. Of these cases, 4 over one year of age have since come in intimate contact with measles and have not contracted the disease and in addition, 2 of the 40 cases were reinoculated at the age of twenty-one and twenty-three months respectively, the result being negative in both. Material for inoculation consists of mucous from the nose of otherwise healthy children taken twenty-four hours before the measles eruption appeared. It was taken on small cotton swabs and kept in glass vials containing a moist piece of blotting paper at the bottom. The inoculations were made by applying the swab gently to the nasal mucous membrane. It would be desirable to devise some method by which the infectious material could be made to retain its virulence for more than twenty-four hours.

Erysipelas Treated with Whole Blood from Convalescent Patient.—A. D. Kaiser (*Arch. Pediat.*, 1915, xxxii, 519) reports a case of erysipelas in a girl, aged six years, which resisted all usual remedies including antistreptococcic serum. The areas involved were the entire left arm, the chest and upper abdomen, and the streptococcus was obtained in culture. Seven ounces of blood were taken from an adult case convalescing from erysipelas and injected, after citration by Zingher's method, into seven different muscles of the child's body. The child's temperature dropped to 100° in twelve hours and to normal within twenty-four hours, accompanied by a disappearance of the redness, swelling and tenderness and a marked general improvement which was rapid and uninterrupted. The adult convalescent's temperature had been normal for five days and the streptococcus had also been grown in culture from the lesions. The protective bodies in the blood of the convalescent apparently acted with success and this method is urged in severe cases where the outcome looks dubious if a suitable donor can be obtained.

OBSTETRICS

UNDER THE CHARGE OF

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The Question of Autoinfection Complicating Pregnancy and the Puerperal State.—ZANGEMEISTER and KIRSTEIN (*Arch. f. Gynäk.*, 1915, civ) had carried out minute clinical studies and observations upon pregnant patients to determine the question of the possibility of autoinfection. Without going into elaborate details regarding their investigations, they conclude that bacteria capable of producing rise of temperature and other disturbance, are present in and about the genital tract of pregnant patients who have never been internally examined; that these bacteria make their way upward into the vagina, so that while they were found in the lower portion in the genital tract in 89 per cent. of cases examined; in 25 per cent. of cases examined they were also found in the upper portion. Clinical studies in the occurrence of fever in patients in whom germs were found in the genital tract before labor showed that these bacteria can undoubtedly produce infection entirely independently of any bacteria introduced during examination or manipulation. These observations have been confirmed by others, so that there is a considerable mass of accurate clinical observation to establish these facts. What are the practical conclusions to be drawn? When we consider the course of spontaneous labor in a normal patient, we find that the escape of amniotic liquid, passage of placenta and membranes, and of the blood and serum which follow, all tend to carry bacteria from above downward and outward. The blood serum which follows the removal of the placenta is the best possible application to the wounds received during labor. So long then as the course is from above downward and the uterine sinuses are promptly plugged by sterile coagula, and the womb remains contracted, the patient should escape serious infection. But frequent examinations, manipulations, and unsuccessful attempts at delivery carry these germs into bruised and wounded tissues, to the cervix and produce infection. In difficult cases where labor has been prolonged much of the success of delivery by addominal section lies in the fact that the infected lower portion of the genital tract is not entered, but that the child is removed through the upper uninfected portion.

External Version in the Treatment of Placenta Previa.—ZALEWSKI (*Arch. f. Gynäk.*, 1915, civ) publishes the results of his observations on this method in the Clinic at Breslau. Out of 192 cases of placenta previa studied, 9 were treated by tamponing the vagina and cervix with iodoform gauze and giving quinin. The maternal mortality was 11 per cent., the fetal mortality 57 per cent., the percentage of puerperal fever 66.6 per cent. In 40 cases the rupture of the membranes was the method employed, in 47.5 per cent. labor proceded spontaneously. There was no maternal mortality and 7 per cent. fetal mortality. These results were obtained among the spontaneous labors only. After the membranes were ruptured, in 21 cases further interference was necessary; in 2 the tampon was used, in 12 combined version and slow extraction, in 7 the use of the dilating bag. By those who use bimanual version with prolonged extraction, the maternal mortality is commonly established at 5 per cent., but the fetal mortality varies from 50 to 84 per cent. Regarding the use of the dilating bag, there is always the uncertainty that while the bag may secure a certain degree of dilatation, spontaneous delivery will not necessarily follow. The patient's strength may become exhausted, or her nervous condition be such that no efficient effort at delivery is made. Under these circumstances the additional manipulation of the bag is a serious danger, and the statistics of placenta previa show that frequent manipulation greatly increases the maternal mortality. The writer calls attention to the value of dilating bags made of animal membrane, such as the bladder of the sheep or pig. These can be rendered thoroughly sterile, can be kept in small flasks ready for use, are less liable to burst than rubber bags, do not undergo such change, are smaller in bulk, and thus can be introduced through a narrow cervix. They are also very cheap. Pressure with a very firm bag in cases of placenta previa seems to be better than with a more elastic rubber bag. The writer also calls attention to the dangers of the puerperal period in placenta previa, and especially from postpartum hemorrhage. In 12 cases of central placenta previa the placenta was manually removed, and 3 of these patients perished from postpartum hemorrhage. To prevent this the writer used secacornin in doses of 2 c.c. combined with similar doses of pituglandol. The intra-uterine tampon was also employed. In 2 cases Momburg's bandage was used, apparently to advantage. It seemed to control hemorrhage until the uterus could be thoroughly tamponed. The writer recognizes the danger of the tampon and urges the general practitioner not to apply the tampon in central placenta previa, to interfere with the patient as little as possible, and to send her promptly to hospital. He seems to have had no experience with delivery by section in these cases and considers it something which is as yet a radical proposition, having a very limited application. Up to the present time the reviewer has treated 22 cases of placenta previa, some of them exsanguinated and brought to hospital by ambulance in emergency, by delivery by abdominal section. All of the mothers have recovered and those children who were in fair condition.

Hunger Fever in the Newborn.—Mayer (*Arch. f. Gynäk.*, 1915, civ) reports studies in newborn infants in Sellheim's Clinic in Tubingen. It is often observed that the newborn infant loses from six to eight ounces during the first week or ten days after its birth. If the loss of weight is rapid the temperature rises and both find their highest point at the third or fourth day, occasionally as late as the sixth day. Some infants show marked thirst during this period. In seeking a cause it is natural to consider the part played by bacteria in the intestine, and also by the passage of urates and uric acid from the kidneys. It is thought when the intestinal condition is not normal that the abnormal bowel permits the absorption of bacteria and toxins which the healthy bowel resists, thus causing the fever. By clinical observation it is found that a mother who has fever does not furnish healthy milk to her child, and this is also true of women suffering from pronounced albuminuria. There is probably a relation between the nourishment of the mother and the condition of the infant's bowel. The effort to furnish infants with sterilized mother's milk lessened, in the Clinic, the number of cases of hunger fever. Such fever still occurred for which there was no adequate explanation. Fortunately these cases are rarely severe or fatal.

The Cause of Chorea Complicating Pregnancy.—ALBRECHT (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) describes the case of a primipara, aged twenty-two years, who was taken with chorea at the beginning of the first pregnancy. Her condition became pronounced and she was treated by intragluteal injection of 20 c.c. normal pregnancy serum. In twenty-four hours the choreic movements had ceased and the patient was much better. She also gained somewhat in weight. He adds the case of a girl, aged sixteen years, in whom chorea appeared at the time when menstruation became established. From the study of these cases he believes that chorea is an intoxication in the pregnant patient with substances formed by the embryo, or in patients at puberty with substances produced by the glands which form the internal secretions.

Icterus of the Newborn an Infectious Disease.—PFALTZER (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) describes a series of cases of what is termed "nuclear icterus in the newborn." This disease shows its most important changes in the nervous system and nuclei of the cerebral tissues, showing yellow discoloration, and also the ganglia. The writer draws attention to the esophagus as the site of infection, probably with the colon bacillus. The fact that children frequently put their fingers and other objects into the mouth readily explains the occurrence of such infection. A toxin produced by the bacillus circulating in the blood would account for the lesions in the muscles and in the nervous system. It is interesting to note that in the muscle fibers some of the most characteristic changes were observed. In this connection it must be remembered that such infection is rarely caused by one germ only, but staphylococci and streptococci may undoubtedly be present. In those cases where it was thought that no infection was present the characteristic changes in the muscle bundles were absent. This condition also calls attention to the frequent infection of the infant from the umbilicus. The practical conclusion of these investigations lies in the necessity for strict asepsis, and that the child's mouth be invaded as rarely as possible.

The Cause of Icterus Neonatorum.—HEYNEMANN (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) has studied icterus neonatorum in the Clinic at Halle, and finds that the cause is primarily a variation in the function of the liver cells in the early days of life. The congested condition of the liver predisposes to this, with the rapid disintegration of the red blood corpuscles. Of this we do not know the precise cause. Evidently anything happening during labor which especially increases pressure upon the child's body forces blood into the liver, or any infection which should attack the blood would produce icterus.

GYNECOLOGY

UNDER THE CHARGE OF

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Diagnosis and Treatment of Vulvovaginitis in Children.—Some very interesting suggestions upon these subjects are made in a recent article by C. C. NORRIS (*Jour. Amer. Med. Assn.*, 1915, lxv, 327). Norris calls attention to the difficulty in demonstrating gonococci in smears obtained in the ordinary manner, from chronic cases, even though the patient may still harbor active organisms. The ability to make such demonstrations is of the greatest importance, however, in determining the point at which the case may be considered cured and treatment stopped, for other theoretical means of determining this, such as the complement-fixation test, have proved entirely unreliable in gonorrheal vaginitis of children. Norris has found the following technique exceedingly valuable for this purpose: The child is placed in an elevated position, so that fluid will not run out of the vagina, and with a soft rubber eye-syringe about a half-ounce of 1 to 5000 bichloride solution, made up in normal salt, is injected. It is important to have the patient in such a position that the vagina will be ballooned out by the atmospheric air. With the vagina thus partly filled with solution and thoroughly distended, a smooth glass rod is introduced and the various parts of the vagina are rubbed with it for the purpose of detaching any adherent secretion. In a further effort to obtain material the solution may be forced in and out a number of times with the syringe. The solution thus obtained is centrifuged for twenty minutes at high speed, and the sediment examined in the usual way. Where this procedure is negative in suspected cases, the following addition is advocated by the author: On the day preceding the bacteriologic examination the entire vagina is painted with a fairly strong silver nitrate solution—5 to 10 per cent., according to the age of the patient—in order to produce a distinct reaction. On the following day washings are obtained in the manner described above, and will often show gonococci when they previously were negative. In 21 chronic cases, Norris says that he obtained positive results in 45 per cent. with ordinary smears, in 75 per cent. with simple washings, and in 97 per cent. with washings preceded by chemical irritation. He does not think it is safe to consider that a cure has been affected until negative findings have been obtained at three consecutive bacteriologic examinations at two-week intervals, no treatment having been employed in the meantime, and the last examination having been preceded by irritation with silver nitrate. With regard to treatment, the author lays great stress on the necessity for perseverance, even in face of the apparent disappearance of symptoms. In the treatment which he has adopted, he depends largely on the well-known fact that dessication quickly destroys the gonococcus. With the patient in the knee-chest or Sims' position, or in the case of an infant, with the buttocks elevated by the nurse, the vagina is ballooned out until it is well distended. In the majority of instances, the hymen should be sacrificed, in order to give more thorough drainage and greater accessibility for treatment. The vagina is thoroughly washed with a weak permanganate solution, and is then swabbed with a 25 per cent. argyrol solution, the latter being employed chiefly as a cleansing agent. After the argyrol has been applied, the vagina is dried thoroughly with a thin strip of gauze, an empty atomizer being used to complete the drying. The child is now left in the Sims position for twenty to thirty minutes, care being observed to keep the vagina well distended with air during this time. As a final step, it is flooded with a weak solution of silver nitrate, starting with 1 or 2 per cent., this gradually being increased as the vaginal mucosa becomes more resistant. These treatments are given three times a week, the vagina being washed out daily by the mother or nurse with a weak permanganate or argyrol solution by means of a soft rubber eye-syringe. Norris admits that this treatment is hardly adapted to dispensary work, owing to the amount of time required. He says that in 14 cases treated in this manner, a cure, as determined by the criteria described above was obtained in an average of twelve weeks, dating the cure from the first of the three negative examinations. The most persistent case lasted eighteen weeks, recurrence having taken place after two negative examinations, gonococci being found in the final test preceded by silver nitrate irritation. In conclusion, the author insists upon the necessity for observing thoroughness and regularity in carrying out the treatment. He believes that the simple instillation into the vagina, often at irregular intervals, of various solutions, as is frequently practised, is of little value in the treatment of the disease.

Pelvic Varicocele.—This subject, which was discussed in this department a year or so ago, has been again brought before the profession in a recent paper by Pinkham (*Amer. Jour. Obst.*, 1915, lxii, 244). He calls attention to the fact that the chief symptom complained of by many women seeking advice for so-called female troubles is a persistent, dull aching pain in the left iliac region, in some instances relieved by the recumbent position, aggravated by standing or walking, and usually worse at the menstrual periods. Often no definite pelvic lesion is palpable. Many of these women are told they have "chronic oöphoritis" or that they have nothing at all the matter; as Pinkham points out, however, the fact is too frequently overlooked that there is always a good reason for physical suffering. Pinkham believes that the true cause of the trouble in many cases of this sort is a varicose condition of the veins of the broad ligament, producing a lesion analogous to varicocele in the male. It occurs much more frequently on the left side than the right, probably because of the fact that on the former side the ovarian vein runs upward and inward to the renal vein, which it enters at right angles; it is very poorly supplied with valves, and anything which would interfere with the free flow of blood would produce venous engorgement. The vein on the right side, on the other hand, has a shorter course, entering the inferior vena cava directly at an acute angle. Pinkham thinks that women who have borne children are more apt to develop a varicose condition of the broad ligament veins than are nullipara, though it may occur in the latter also. Subinvolution of the uterus, loss of support due to lacerations of the birth canal, and retroversion of the uterus all tend to favor venous stasis in the parturient woman, while an adherent sigmoid, with associated constipation, may be the underlying factor in a nullipara. The author strongly believes that if more attention were paid to the possible existence of pelvic varicosities, the results of surgical intervevtion in cases of indefinite pelvic pain would be vastly improved. The diagnosis, he admits, must often be made by elimination. The treatment he advises is double ligation of the varicosities, with excision of the intervening area. He reports a number of cases in which this procedure has been carried out, apparently with exceedingly favorable end-results.

Repair of the Ureter with Small Intestine.—An interesting case is reported by BARBAT (*Calif. State Jour. Med.*, 1915, xiii, 70), in which an extensive ureteral injury was repaired by means of a segment of intestine, and a kidney thus saved that would otherwise have had to be sacrificed. The patient was a woman, aged thirty years, who a few months before coming under Barbat's observation had undergone an operation for extensive pelvic inflammatory disease, with widespread adhesions and much distortion of the normal relations. The operator had inadvertently included the right ureter in one of his sutures. A collection of urine formed in the region of McBurney's point, and was evacuated by a superficial incision, following which a urinary fistula formed at this point, and continued to discharge. At a subsequent operation about 1½ inches of the ureter were found to be lacking; an unsuccessful attempt was made to form a new ureter by sewing adjacent tissues around a ureteral catheter introduced from the bladder, but this produced no improvement in the condition. When first seen by Barbat, the patient presented a small fistula in the region of McBurney's point, through which clear, bacteria-free urine was constantly discharged. Indigo-carmine appeared here at about the same time as from the left ureteral orifice in the bladder; it seemed probable, therefore, that the right kidney was functionally unimpaired, and worth preserving, if possible. At operation, numerous intestinal adhesions were separated, after which the ureter could be traced down to a mass corresponding to the bottom of the fistula. It was ligated and cut close to this, the proximal end being lifted up and temporarily clamped. A loop of ilium about 7 inches long was then isolated, continuity of the intestinal tract being reëstablished by means of a Murphy button. Great care was taken to see that the blood supply of the isolated segment was not interfered with, and that undue traction was not made on its mesentery. It was flushed out with a large amount of 1 to 1000 formalin solution, and the upper end closed by inversion. The lower end was sewed to a slit in the bladder by continuous through-and-through sutures. A small oblique puncture was then made in the side of the intestine near the closed upper end, and the ureter anastomosed into this by the same technique as is commonly employed in ureterovesical implantation. The patient had a rather stormy convalescence, and for a time urine was discharged from the old fistula, as well as from a new one which formed in the abdominal scar. These fistulæ eventually closed, but not until three and seven months respectively, after operation. The patient has since gained 25 pounds in weight, and is in excellent health three years later, although at the last examination the bladder urine showed the presence of some colon bacilli and shreds of mucus.

OTOLOGY

UNDER THE CHARGE OF

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Experimental Investigation Concerning the Influence of Ethyl and Methyl Alcohol upon the Organ of Hearing. A Contribution to the Pathogenesis of Neuritis Acustica Alcoholica.—The deleterious effect of many drugs upon the organ of hearing is well known and the results of the ingestion of quinin and salicylic acid and of various arsenical combinations, in this respect, have been frequently demonstrated. Of the effects of such other substances as chenopodium oil, lead, silver and mercurial salts, phosphorous and carbonic acid but little is definitely known and our knowledge of the effect of alcohol upon the ear is equally imperfect, begin confined, according to the author, mainly to the results of occasional and imperfect clinical observations and of two lines of experimental pathological investigation. The protracted consumption of alcohol may result eventually, as has been demonstrated, in inflammation and degeneration of the auditory nerve, but notwithstanding the extent of alcoholism, alcoholic polyneuritis is of comparatively rare occurrence and especially so as exhibited in the auditory nerve. Marian and Ostmann have shown that alcohol has a lesser affinity for the auditory nerve than the drugs previously mentioned and that the deleterious influence of alcohol is much more frequently exhibited in other than the auditory nerve, especially the optic nerve. Zytowitsch gives as the results of his investigations in alcohol poisoning in rats and guinea-pigs changes exhibiting themselves first in the ganglion spirale, next in the efferent nerves in the lumina spiralis ossea and, finally, in the organ of Corti, the basal whorl being the last and the least affected. Hemorrhages were notable in all cases, less frequently in the endolymphatic portion; the vestibular region was also included in the area of these ecchymoses. Tadokoro found as the result of his investigations in the majority of his cases an osteoplastic labyrinthitis and the author refers the hemorrhages in the first instance to postmortem changes and the labyrinthine showings in the second instance to suppurative infection from the middle ear. The clinical studies of Marian and the supplementary clinical contributions of Zytowitsch refer the aural changes incident to alcoholism, both chronic and acute, to the labyrinth, and as exhibited, preponderatingly, in men between twenty-five and fifty years of age. In no instance was there opportunity for postmortem evidence of the clinically inferable labyrinthine changes. Under these circumstances, YUTAKA NAKAMURA (*Passow and Schaefer's Archiv*, December, 1914), undertook a series of carefully conducted investigations into the labyrinthine conditions incident to alcoholic poisoning, using for his material only carefully selected guinea-pigs all of whom were previously examined as to hearing by the method of Preyer, auricular reflex, and as to the integrity of the vestibular function by the caloric test. The alcohol, usually 40 per cent. strength, was administered by means of a soft rubber catheter passed into the stomach, the jaws of the animal being controlled by a mouth clamp, devised by the author and consisting of two S-shaped metal rods or tubes controlled by a set screw, the risk of internal injury to the animal in process of administration of the alcohol being thus minimized; in one series of cases acute poisoning was ensured by large doses, in a second series, a chronic effect was produced by daily administration in small doses, the clinical symptoms of the poisoning usually manifesting themselves within ten minutes, though this, and the degree of effect, proportionately, varied greatly in individual cases. The nutrition of the subjects was regulated according to the daily determination of the body-weight in order to secure as nearly as possible an assumed mean of nutrition. The evidences of the intoxication in both the acute and the chronic cases corresponded to those commonly observed in the human subject, but at no time throughout the experiments, except during the toxic periods, was there any determinable decrease of hearing or of the vestibular function. The method of preparation of the material was, in the main, that of Yoshii with certain minor modifications, but including fixation with the brain *in situ* and the acusticus and medulla undivided, and, throughout the examination, especial care was taken in other and similar respects to avoid traumatic postmortem results which might serve to confuse the conclusions to be drawn from the actual changes in an auditory apparatus of such exceeding delicacy. In conclusion, the author says that both ethyl and methyl alcohol have an injurious effect upon the ear, and especially upon the auditory nerve, the three components of the peripheral cochlear system being more frequently and more severely affected, nerve fibres, ganglion cells and cells of Corti, than the vestibular and facial nerves, pathological changes in the vestibular and geniculate ganglia being in no instance found. The alcohol attacks, as a nerve poison, only the neural elements of the organ of hearing, all the remaining tissues in the middle ear and labyrinth, including bloodvessels and bony structures remaining unaffected. The pathological changes in the acoustic system of the auditory nerve consist mainly in degenerative, atrophic processes with segmental destruction of the cochlear fibres, degenerative implication of the spiral ganglion cells and the cells of Corti without corresponding evidence of inflammation, these degenerative changes being, moreover, more pronounced in the peripheral portion of the cochlear nerve, in the fibrils of the lamina spiralis ossea and in the modiolus than in the cochlear trunk itself, the changes in the spiral ganglion cells of the upper cochlear whorl being more pronounced than in the lower portion. These investigations seemed to prove that the hematogenous changes in the cochlear nerve occurred, in the three portions of the system almost coincidently, in cases of acute alcoholic poisoning, whereas the cells of Corti, in the more chronic cases, remained sometimes unaffected and that the hemorrhages in the middle ear and labyrinth observed by Zytowitsch were the result not of poisoning, but of an extrinsic trauma.

Parotid Fistula in the External Auditory Canal.—The first case of this kind was described by Politzer, in 1906, and that of KRETSCHMANN (*Arch. f. Ohrenh.*, xcvi, 8) is similar in that, in both cases, the symptom occurred in otherwise entirely normal ears without evidence, moreover, of parotid disturbance, suddenly without pain and without other than the immediately induced sensation, an outflow appeared from the ear. Otoscopic examination revealed a swelling upon the canal wall about 4 millimeters in diameter, in the author's case, on the anterior superior and, in the case of Politzer, on the inferior bony canal wall, this swelling expanded and subsided coincidently with the movement of the jaw in chewing; at its base an opening in the bony canal wall could be determined by means of a probe, the swelling being, in fact, a hernial protrusion filled either with fluid or with glandular tissue. In neither case did the history give a clue to the origin of the aural manifestation. Politzer regarded it in his case as a cystic extension of the parotid which had burst through the membrane closing the opening due to a dehiscence of bone in the canal wall; the treatment consisted in rest and in cauterization of the projected area.

The Pathogenesis and Treatment of Otosclerosis. — DENKER (*Deutsch. med. Wchnschr.*, 1914, xix) denominates as otosclerosis a group of cases in which, with patent tympanopharyngeal tubes and nearly normal aspect of the drum-heads, the clinical picture is presented of a progressive, definitely determinable, by functional examination, steadily increasing, difficulty in hearing. Structurally, there is an increasing immobilization of the stapes, spongiosity of the labyrinth capsule and, sequent thereto, atrophic degenerative changes in the nerve end apparatus of the labyrinth. Etiologically, the question as to whether the otosclerosis is secondary to a disorder of the tympanic mucosa or originates primarily in the bony capsule is not yet decided, but the majority of authorities incline to the latter view, in some instances the otosclerosis being regarded as typical of rheumatic arthritis. Furthermore, the incidence and progress of the spongiosity and whether it is of inflammatory origin or otherwise has not yet been determined. It is evident from all statistical evidence that the preponderating number of cases occur in women and the author suggests that gestation has a distinct bearing upon the beginning of an otosclerosis, or upon its subsequent progress and that the function of the hypophysis cerebri may come to be found to have a bearing upon the existence of this aural condition. Another view which has its adherents is that the otosclerosis has its origin in a disorder of the circulatory system and it is certainly true that hereditary predisposition is apparently an important factor, while syphilis and tuberculosis are of comparative importance etiologically The therapeusis of otosclerosis is practically powerless, as might be inferred from the pathological findings and from the results of attempts at treatment by means of radium, electromotor massage and varied internal medication.

PATHOLOGY AND BACTERIOLOGY

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A Remarkable Finding of Anthrax Spores in the Earth of a Burying Place.—The resistance of anthrax spores in infected earth is of the greatest hygienic importance. W. v. GOZENBACK (*Ztschr. f. Hyg. u. Infektionskrankh.*, 1915, lxxix, 336) reports the finding of anthrax spores in the earth of a place which had been used six years before for burying diseased animals. The place was wanted as a playground and the investigation was undertaken to determine whether it was safe for such use. The author recovered anthrax bacilli six times by animal injections and twice by direct plating. One ear gave four positive findings at the surface and from depths of 1.3 and 2 meters deep. Earth worms from these regions gave negative results. A cow buried in this particular place had been slaughtered there and remained twenty-four hours before burying. Moreover, the temperature at this time was 18° to 21° C. These facts led the author to conclude that the earth had been badly infected from the blood and body fluids of the slaughtered animal and that the bacilli in the soil thus polluted and under conditions of favorable temperature had actually grown. Many of the guinea-pigs used in these experiments appeared to have died from malignant edema and the confusion liable to arise from the resemblance of the two diseases and the morphology of the bacilli must be controlled by cultures.

Observations on the Antibacterial Action of Coins on Media.—NATONEK and REITMANN (*Ztschr. f. Hyg. u. Infektionskrankh.*, 1915, lxxix, 345) carefully review the literature on the action of different metals against bacteria. Many theories have been advanced. The theory given us as a result of their own experiments is that the metal exerts a direct action upon the bacteria. Electric currents between the metals, through the water of condensation of the media, bring about solution of the metal. Small particles of the metal in the moisture of the media are probably held in suspension. The oligodynamic activity against bacteria of solutions of the heavy metals is well known. The addition of insoluble substances to such a solution lessens or destroys the bactericidal action. The authors found in their experiments that when coins were placed on plates seeded with bacteria no growth occurred under or in a circle surrounding the coin. This has been shown by many other observers. They further showed that when a coin was placed on an agar plate for a few hours and then removed the area under and about the coin showed no growth after smearing the plate with bacteria. If chalk or India ink were added to the plate before treatment with the coin no bactericidal action resulted. The same is true if the plate is very heavily seeded. When the coin was left on the plate for a long time (five days) and the plate then seeded, no interference with growth was found. This latter result the authors explain on the dilution of the substance or its alteration by oxidation. The other findings confirm the theory of the oligodynamic action of metals in solution. Agar treated with copper and silver coins was tested and copper was found in both cases and only a trace of silver from the silver coin.

Experimental Study of Distribution and Habitat of the Tetanus Bacillus.—The tetanus bacillus has been found most widely distributed in nature, from the mud of Lake Geneva and water of the Dead Sea to the arrows of the natives of New Herbrides. Its presence in dust, soil, wearing apparel, gun wads, and feces is of common knowledge. NOBLE (*Jour. Infect. Dis.*, 1915, xvi, 132) studied the distribution of tetanus bacilli among the herbivorous animals, particularly through the fecal excreta. The excreta of horse, cows and guinea-pigs were analyzed by the use of Smith's anerobic method. The horses showed the presence of these organisms in 18 per cent., but no tetanus bacilli were found in the material from cows. In feeding tetanus organisms to guinea-pigs the spores were recovered on the seventh day after feeding. They found that animals having the organism in the intestine may, during certain seasons of the year, be free from infectinon. Some experiments show that the bacilli actually multiply while in the bowel. Those animals in which the bacilli appear normally may act as carriers for this organism and infect large areas.

The Effect of Industrial Dusts in the Production of Respiratory Diseases.—The importance of dust of various kinds as causative factors in respiratory diseases is being borne in upon us with greater weight. HEIM and AGASSE-LAFONT (*Arch. gén. de méd.*, 1914) after reviewing the various ill-effects of industrial dusts came to the conclusion that the classification should not rest upon the origin of the dust but rather upon the nature of its harmful influence. They recognize dusts of an active and passive nature. The effects of the first are toxic, predisposing or infectious, while the dusts acting passively act by their mere presence as foreign bodies upon the surfaces of the respiratory system. These passively acting materials may be of soft or hard consistency. The latter are more effective in bringing about the common chronic pneumokoniosis. They point out that the active agents are by far the most important in bringing about the acute respiratory diseases of which pneumonia and acute bronchitis are the most frequent. They do not follow the chronic lesions resulting from the passive agents to a conclusion to illustrate the increased predisposition of the damaged tissues to other secondary processes.

Therapeutic Leukocytosis.—The first appreciation of quantitative changes of leukocytes were observed in infectious diseases. Its common occurrence in infections brought forth many hypotheses of its development. Many believed that the bacterial toxins were directly responsible for leukocytosis and compared its occurrence with the experiments of Metchnikoff in which leukocytes actively combated the introduction of arsenic and other poisons into the body. In fact, the activity of leukocytes toward various poisons was demonstrated in connection with a variety of synthetic organic compounds. On the other hand, new views indicated an activity of leukocytes, not by a mere absorption of the poison, but by an elaboration of secretions which are antagonistic to the foreign substances. This argument has been much used in the discussions on immunity. The underlying factor in chemotaxis is not clear. It is evident that leukocytes are not equally attracted by all forms of infection, some types even causing them to disappear from the blood. There are some, however, that believe that the appearance of leukocytes in the blood is dependent upon their active discharge from the lymph channels while others believe that it is controlled by the activity of the bone-marrow. Many points governing the presence of leukocytes in the blood are not clear and it would appear that under different conditions different factors are active in determining their increase in the blood. In general, however, it would seem that the presence of increased members of leukocytes is related to their activity against toxins and bacteria, in the production of antibodies against these substances or in being driven from their natural sources (spleen, bone-marrow and lymph glands). The very fact that leukocytes bear such a close relation to the favorable results occurring in infectious diseases has suggested the institution of therapeutic measures, whereby a leukocytosis might be induced. This is far from being an untrodden field, for many authors have demonstrated an artificial leukocytosis through various substances. Although the list of substances which have been made use of is long, there are few of them which stand the practical test. In the majority of instances, the demonstration of an increased number of leukocytes after the use of a certain material has seemed sufficient evidence of its value. The control, however, by many tests among numerous patients or normal individuals has seldom been undertaken. Moreover, the experiments have shed but little light upon the manner in which the cell increase has taken place. GEHRIG (*Ztschr. f. exper. Path. u. Therap.*, 1915, xvii, 161) studied the action of various antipyretics which are commonly considered to stimulate leukocytosis. He was unable to demonstrate any such definite change in the blood of patients under observation. There was likewise no alteration in the relative percentage of the various leukocytes after treatment.

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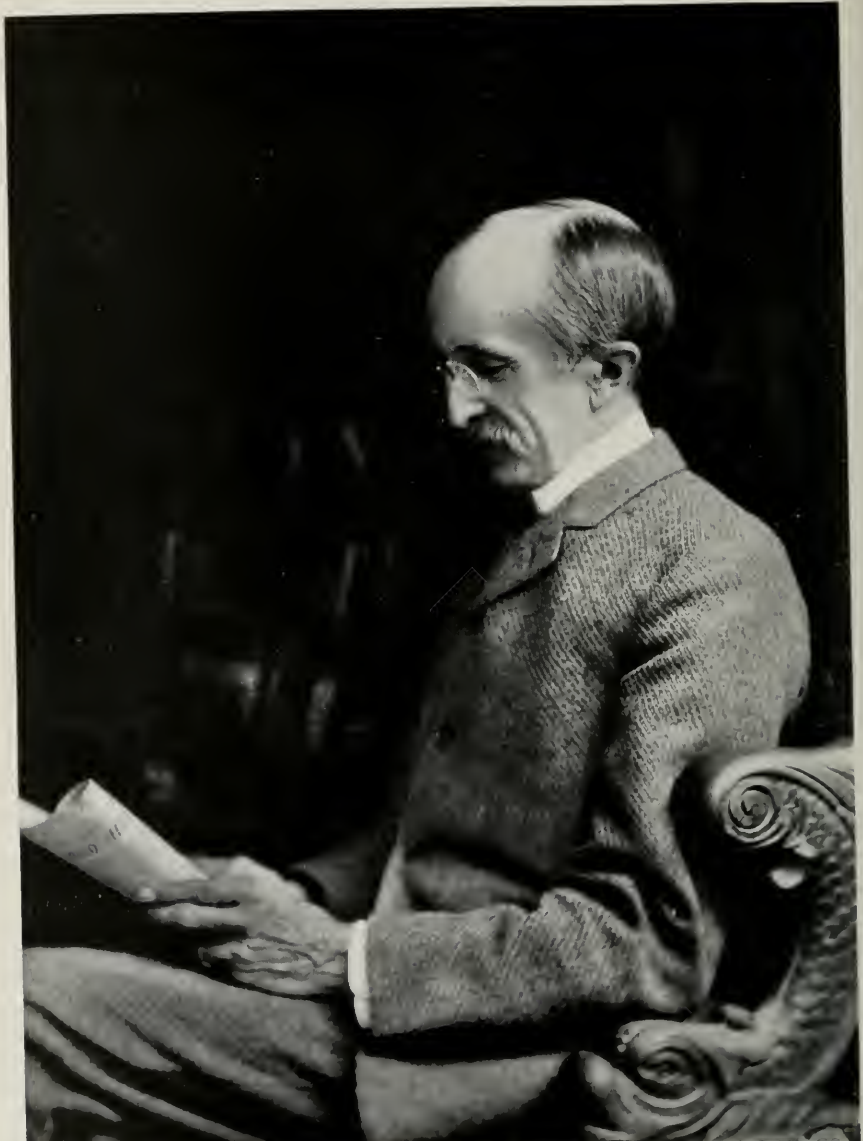

E. L. Trudeau

EDWARD LIVINGSTON TRUDEAU, M.D.

I FIRST saw Dr. Trudeau in the summer of 1888, and when I last saw him in the end of August, 1915, scarcely more than two months before his death, I found him surprisingly unchanged in the twenty-seven years that had elapsed. It was in 1872 that he was carried into the Adirondacks—brought there, as he often said, to die. Yet in the forty-three years since then he has done an amount and a quality of work equalled by very few men who call themselves healthy.

In 1888, when I first saw him, he was splendid to look at. His upright, trig, military carriage, his fine, resonant voice, the warmth and beauty of his smile, struck everyone at first glance. These three attributes he preserved even to the end of his life. They were all manifestations of his unquenchable courage. The most remarkable thing about Dr. Trudeau, as I see it, was his stupendous, one might say his supernatural, bravery. Exiled to the Adirondacks in an apparently hopeless stage of tuberculosis, without laboratory instruments, training, or scientific comradeship, he built up the first research laboratory in the country dealing with the problems of tuberculosis. Only those who have tried to do laboratory work alone can appreciate the sort of courage that this needed. Yet he has often spoken of it to me as something done chiefly in self-defense. Without the continuous and secure interest of laboratory work he could not have faced undaunted the task of dealing day after day with hopeless cases of tuberculosis—for at the start of his work he saw very little else. People had not then learned to seek treatment in the more favorable stages of the disease. He always thought of the laboratory as a refuge and solace for himself and other consumptive physicians exiled at Saranac.

Hardly secondary to the stupendous feat of building up this laboratory, which was finally established and given a name in 1894, though he had worked at it long before that by himself, was the feat of starting without money or precedents to guide him, the first sanatorium for the impecunious consumptive. Though I have put this second in importance, as compared with his laboratory adventure, it was in fact begun in 1884, ten years earlier. That is a long time back in the history of our efforts against tuberculosis in this country. The first State sanatorium for tuberculosis was not opened until 1896, twelve years later. In two great directions of effort, then, scientific and philanthropic, Trudeau was a pioneer. In his prime he was active also in many other directions. When I first knew him he was really the uncrowned King of the Adirondack region, a crack shot, an enthusiastic hunter, interested in every project and every personality in the mountains. No decision of importance could be made without his counsel. Nothing was settled or secure until his judgment had been passed upon it.

Some of us remember how only a few years ago he came down to Washington at the time of the Congress of Physicians and Surgeons to read his memorable address on "Optimism." Optimism from the lips of a man who had everything to discourage and dishearten him is indeed an inspiring gospel. It proved also in his case a potent stimulus to health and vitality. Again and again, when everyone else would have given him up as hopelessly ill, he came back again and again to life and activity, until Dr. Osler came to speak of him as "doing the Phœnix trick once more." Last August, in one of the brief periods of renewed life and activity, he was eagerly planning a postgraduate medical school for the clinical study of tuberculosis at Saranac—he at the end of his forty-three years of struggle against tuberculosis, and less than three months from his death!

It is a great satisfaction to know that he had finished at that time his autobiography, passages of which he then read to me. It is full of his own unique personality, and will preserve for us all one of the most precious and inspiring memories of our lives. To me he is especially inspiring, because his life was throughout built upon a Christian basis. Patients soon came to know that his help was as priceless in the closing hours of life as at any other period. Men needed him to help them live and to help them die. Trusting him first as a man, they came to depend upon his Christian optimism and his Christian hopes.

Richard C. Cabot.

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ORIGINAL ARTICLES

OBSERVATIONS UPON COMPLEMENT-FIXATION IN THE DIAGNOSIS OF PULMONARY TUBERCULOSIS.[1]

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In the following contribution I shall give the results of certain experiments upon complement-fixation in tuberculosis that have been made in this laboratory during the past year, and that appear to indicate that in this method we possess a valuable aid in the diagnosis of active tuberculous infection and a guide as to the results of therapeutic measures.

The method of applying the test as detailed in this report is not claimed to be perfect by any means, for further research will undoubtedly result in improvements both in technic and results; but as it has given, in my hands, results closely comparable with those obtained with the Wassermann test in syphilis, it is believed that a description of the method is justified. It is hoped that others, who are more favorably situated for work upon this subject may consider the results obtained with this test encouraging enough to warrant further research, and that, as the result of such research, a method will be evolved that will be practical and easy of application, and that will enable us to diagnose tuberculosis in its earliest stages.

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[1] Published with authority of the Surgeon-General, United States Army.

Historical. It would be unprofitable to review here the very numerous attempts that have been made in the past to perfect a method of complement-fixation in tuberculosis that would give uniform and accurate results, and that would be of service in the diagnosis of the disease. Although it was the studies of Wassermann and Bruck upon complement-fixation in tuberculosis that first induced them, together with Neisser, to investigate the possibility of working out such a test in the diagnosis of syphilis, an effort rewarded by the discovery of what is now known as the Wassermann test, up to the present time no method of complement-fixation in the diagnosis of tuberculosis has been generally accepted as of much value by the medical profession.

The researches of Citron appear to demonstrate that after the injection of tuberculin, antibodies are formed capable of binding complement; but the production of these antibodies is transitory, and they soon disappear from the blood serum. Likewise, it has been suggested that during an active tuberculous process complement-binding bodies may be present in the blood serum, but only in small amount, and at varying intervals, while they entirely disappear if the tuberculous process becomes quiescent. Aside from the question of the discovery of a suitable antigen, it has been quite generally held that a complement-fixation test in tuberculosis could never be of practical value because of the variability in the presence of suitable antibodies in the blood serum and in their amount.

However, the consensus of opinion of late appears to be that with a suitable antigen one should be able to devise a complement-fixation test for tuberculosis that would give useful results. This opinion has lead to the study of antigens that might be used in such a test, and for this purpose various substances have been used, as watery and alcoholic extracts of tuberculous organs, either alone or combined with some form of tuberculin; tuberculin alone; tuberculin filtrate; watery extracts or emulsions of the tubercle bacillus; and mixtures of various tuberculins. With the exception of the antigens described by Besredka and by Hammer, no very practical results have been obtained with any of those mentioned.

The antigen recommended by Besredka,[2] consisting of a suspension of bacterial substance derived from dried and ground tubercle bacilli, and that of Hammer,[3] consisting of an alcoholic extract of tuberculous tissue to which has been added a certain amount of old tuberculin, appear to have given very consistent results; but, unfortunately, reactions have occurred with these antigens in other conditions, especially in syphilis, and in a considerable proportion of the cases tested.

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[2] Compt. rend. Soc. de biol., 1914, lxxvi, 180.

[3] Münch. med. Wchnschr., 1912, lix, 1750.

In a recent very valuable study by Bronfenbrenner[4] the results are given of experiments made with the antigen of Besredka in the diagnosis, by complement-fixation, of tuberculosis. He found that in active tuberculosis he obtained 93.8 per cent. of positive reactions; in convalescents presenting no symptoms of the disease, 55.5 per cent. of positive results; while in cases strongly suspected of tuberculosis but in which no definite diagnosis has been made, 75 per cent. gave a positive reaction. However, in treated and untreated cases of syphilis he obtained 24 per cent. of positive reactions with this antigen and 8 per cent. of his controls reacted positively. He found that he could separate from Besredka's antigen the substance or substances giving positive reactions with syphilis and other conditions, and that this purified antigen apparently was specific for tuberculosis. In regard to certain negative reactions obtained in undoubted active tuberculosis he states that they suggest that in certain stages of the infection the circulating antibodies apparently disappear from the blood.

Several other investigators have reported very favorable results with Besredka's antigen, notably Inman,[5] who obtained 95 positive reactions in 100 cases of active tuberculosis; and while these reports are very encouraging, the large percentage of syphilitics that react positively with this antigen militates against its use as a diagnostic agent. On the other hand, the method described in this paper does not possess this disadvantage, for the antigen employed does not give positive results with the blood serum of syphilitics in the absence of coincident tuberculous infection.

Technic and Material. The general technic of the complement-fixation test for tuberculosis experimented with is that employed in making the Wassermann test in this laboratory, and which I have described fully in previous contributions.[6 7 8]

The *antigen* employed consists of an extract of several strains of the human tubercle bacillus, prepared as follows: The various strains of the bacilli are grown on a liquid medium composed of alkaline bouillon to which a teaspoonful of egg white and egg yolk has been added to each 250 c.c. of the bouillon. After growth is well advanced, an equal amount of 95 per cent. alcohol is added to the culture, and the whole shaken in a shaking machine for twelve hours; the mixture is then allowed to stand in an incubator at 37° C. for twenty-four hours, after which it is again shaken for six hours and filtered through a very fine filter paper or through a Berkefeld or other equally good filter. It appears to make no difference whether the mixture be filtered through a paper or through the Berkefeld so far as antigenic properties are concerned. The filtrates of the strains cultivated are mixed together and the resultant mixture titrated for anticomplementary, hemolytic, and antigenic qualities. The undiluted mixture should be titrated first, as in my experience it is seldom necessary to dilute the mixture.

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[4] Arch. Int. Med., 1914, xiv, 786.

[5] Compt. rend. Soc. de biol., 1914, lxxvi, 251.

[6] Craig, C. F., Jour. Exper. Med., 1910, xii, 726.

[7] Craig, C. F., Jour. Infect. Dis., 1911, ix, 213.

[8] Craig, C. F., and Nichols, H. J., Studies of Syphilis, Bull. No. 3, War Dept., Office Surg.-General of Army, 1913, lxxii.

An antigen may also be prepared by carefully transferring a portion of all of the strains used to a large culture flask, planting each strain far enough apart so that it may be observed whether growth occurs. Generally one or more of the strains transplanted in this manner fail to grow, but this can be disregarded if one works with eight or more strains. When growth has occurred to a considerable extent the alcohol is added, as already described, and the antigen prepared in a similar manner. Antigens made in this way appear to be slightly stronger in antigenic content than when the filtrates of the separately cultivated strains are mixed, but the greater difficulty of cultivating so many strains of the bacillus together more than offsets the slight gain in complement-binding power.

The antigen must be kept in the ice-box except when a small portion is removed for use in the test, as exposure to room temperature, even for a short time, markedly lessens its antigenic properties. It is also necessary that the greatest care be taken that all utensils used in the preparation of the antigen are sterile.

The preparation of a polyvalent antigen for use in this test was suggested by the fact that there are modifications of both the human and bovine types of tubercle bacilli and that some strains of the organisms differ from others in infective power and in cultural reactions. It is probable, indeed, that by adding strains of the bovine bacillus to the antigen, better results will be obtained than when the human strains alone are used, and this subject is now being investigated. It is also believed that a polyvalent antigen prepared by extracting the various strains of the bacillus grown upon solid media, using only the bacterial growth, will probably prove as accurate as the antigen described, and, if, so, it will greatly simplify the method of making the antigen.

A human *hemolytic* system was employed in the test, the amboceptor being obtained by injecting rabbits with human red-blood corpuscles in the usual manner, and the *blood suspension* used consisted of a 1 per cent. suspension of human red-blood corpuscles in normal saline solution. As *complement* guinea-pig blood serum was employed, and this was invariably titrated just before use. The blood sera tested were inactivated at 56° C. for one-half hour before testing, and the final reading of the test was generally made an hour after taking the specimens from the water-bath.

The methods of preparing and titrating the various reagents and the technic of performing the test were the same as in the

Wassermann test as made in this laboratory, and have been fully described elsewhere.[9]

Material. Through the kindly assistance of Colonel Bushnell, Medical Corps, U. S. Army, commanding the U. S. Army General Hospital at Fort Bayard, and Lieutenant Callender, who collected the specimens, I was able to test the blood of 166 patients in that institution suffering from pulmonary tuberculosis. In addition, the blood of 150 syphilitics as well as of 100 patients suffering from other diseases was tested, and also 150 normal individuals who were used as controls.

Method of Reading the Results of the Test. The final result of the test was read from an hour to two hours after the last incubation in the water-bath, and this is important, as otherwise some of the positive reactions may become weak or negative. If left in the ice-box over night many of the strongest positive reactions are negative in the morning. Accurate results can only be obtained by reading the test within the time specified.

Early in the work it was determined to estimate the strength of the reaction in tuberculosis in the same manner as the Wassermann test in syphilis, in which the results have been recorded as double-plus (++); plus (+); plus-minus (±); and minus or negative (−). When complete inhibition of hemolysis is obtained the result is recorded as double-plus; when less than 50 per cent. of the blood corpuscles are hemolyzed, as plus; when more than 50 per cent. are hemolyzed, as plus-minus; and if complete hemolysis occurred as minus, or negative. However, it was quickly found that many cases of tuberculosis gave very strong plus reactions, so that it early became evident that a plus reaction with this test was diagnostic of tuberculosis, as it did not occur in other diseases or in healthy individuals. On the other hand it was also found that a plus-minus reaction sometimes occurred both in other diseases and in normal individuals, so that this type of reaction had to be considered as practically negative. In considering the results of the test as here given it should be understood that a positive result includes both double-plus and plus reactions, while a negative includes both plus-minus and minus reactions.

As regards the relative number of double-plus and plus reactions it may be stated that of the 142 cases of pulmonary tuberculosis that reacted to the test, 119 gave a double-plus reaction and 23 a plus reaction; of the 103 cases of active infection reacting, 87 gave a double-plus reaction and 16 a plus reaction; while of the 39 inactive cases of infection, 32 gave a double-plus reaction and 7 a plus reaction. Owing to the percentage of tuberculous cases giving a plus reaction, the test as at present developed requires very careful titration of all the reagents and experience in reading the results of hemolytic reactions.

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[9] Craig, C. F., and Nichols, H. J., Studies of Syphilis, Bull. No. 3, War D pt., Office Surg.-General of Army, 1913, lxxii.

The tests made in this laboratory in the study of this subject may be divided into three groups, as follows: Group 1. Cases in which the diagnosis was pulmonary tuberculosis, either active or inactive. Group 2. Cases in which the diagnosis was of some other disease. Group 3. Normal individuals.

Results of the Test in Group 1. In order to understand the results of the complement-fixation test and their significance in this group it is necessary to briefly describe the classification of the cases tested, which is that followed at the U. S. Army General Hospital at Fort Bayard, New Mexico.

The cases tested were divided into three general classes: Class 1, including incipient cases of tuberculosis; Class 2, moderately advanced cases; and Class 3, far-advanced cases. In addition the cases were classified as *active* and *inactive,* and, again, with reference to the extent of the involvement of lung tissue as *Involvement 1,* indicating a slight lesion extending at most to the volume of one lobe or two half-lobes; *Involvement 2,* slight lesion extending further than *1,* but at most to the volume of two lobes or a severe lesion extending at most to the volume of one lobe; and *Involvement 3* including all lesions which in extent of the parts affected exceeded *Involvement 2.*

The total number of cases of pulmonary tuberculosis tested was 166,[1] of which 142, or 85.5 per cent., gave positive results, and 24, or 14.4 per cent., gave negative results.

The cases were divided as regards the nature of the infection into *active* and *inactive* infections, and the following table gives the results of the test in each class:

TABLE I.—RESULTS OF THE COMPLEMENT-FIXATION TEST IN PULMONARY TUBERCULOSIS WITH REFERENCE TO THE ACTIVITY OF THE INFECTION.

Total cases.	Active.	Inactive.	Positive.	Per cent.	Negative.	Per cent.
166	107	. .	103	96.2	4	3.7
	. . .	59	39	66.1	20	33.8
	107	59	142	85.5	24	14.4

From the foregoing table it is evident that the percentage of positive results obtained with this test in active tuberculous infection was much higher than in the cases classed as inactive, 96.2 per cent. of the active cases giving positive results, while only 66.1 per cent. of the inactive cases reacted to the test. It should be remembered that the classification into active and inactive cases is entirely clinical, and that many of the cases giving a positive result in the inactive class were merely quiescent and may or may not have shown the bacilli in the sputum.

The percentage of positive results in active tuberculous infection of the lungs, *i. e.*, 96.2 per cent., is as high as that obtained in my experience with the Wassermann test in secondary syphilis, for in 1969 cases in that stage of the disease I have obtained positive reactions in 96.1 per cent. of the cases. This speaks very favorably for the accuracy of this test in the diagnosis of active tuberculous infection, and indicates that in this class of cases we may expect as good results with it as are obtained with the Wassermann test in secondary syphilis.

The percentage of positive results in clinically inactive tuberculous infection is practically the same as that I have obtained in latent syphilis with the Wassermann test. In the clinically inactive cases of tuberculosis, 66.1 per cent. gave a positive reaction, while in 1354 cases of latent syphilis I have obtained 69.4 per cent. of positive results.

The importance of the comparatively large percentage of positive results in clinically inactive tuberculosis consists in the demonstration of the fact that the infection in these cases was not really inactive, if we believe that complement-fixing bodies in the blood indicate an activity of the infection. In the past it has been generally accepted that such bodies were not demonstrable in the blood serum unless tuberculosis was clinically active; but the results of this test prove that such bodies can be demonstrated when the disease is inactive clinically. For this reason it would appear that a positive reaction indicates an active focus somewhere in the body and that the test will prove of value in differentiating really cured infections from those which are simply quiescent.

Relation of the Results to Class of Patients Tested. It has been stated that the cases of pulmonary tuberculosis tested were divided into three classes: incipient cases, advanced cases, and far-advanced cases. It was found, as would be expected, that the highest percentage of positive results was obtained in patients in whom the infection was furthest advanced, as is shown in the following table:

TABLE II.—COMPLEMENT-FIXATION IN TUBERCULOSIS IN RELATION TO THE CLASS OF INFECTION.

Class.	Character of infection		Positive reaction.	Per cent. positive	Negative reaction	Per cent. negative.
	Active.	Inactive.				
1. Incipient cases	1 . .	. . 24	1 14	100.0 58.3	0 10	0.0 41.6
Total, 25	1	24	15	60.0	10	40.0
2. Moderately advanced cases	53 . .	. . 32	51 22	96.2 68.7	2 10	3.7 31.2
Total, 85	53	32	73	85.8	12	14.1
3. Far advanced cases . .	53 . .	. . 3	51 3	96.2 100.0	2 0	3.7 0.0
Total, 56	53	3	54	95.4	2	3.5

While in the foregoing table the percentage of positive results happens to be the same for active infections in both moderately advanced and far-advanced cases, in the inactive infections the positive percentage is much greater in the far-advanced cases, and in the incipient cases the percentage of negative results is higher than in either the moderately advanced or far-advanced infections.

The relation of the results of the complement-fixation test to the amount of lung involvement is shown in Table III, where the infections are arranged in accordance with the amount of involvement, as previously defined.

TABLE III.—COMPLEMENT-FIXATION IN PULMONARY TUBERCULOSIS IN RELATION TO THE AMOUNT OF LUNG INVOLVEMENT.

Nature of infection.	Involvement.			Positive reaction.	Per cent. positive.	Negative reaction.	Per cent. negative.
	1	2	3				
Active	29	..	..	27	93.1	2	6.8
	..	30	..	30	100.0	0	0.0
	..	..	48	46	95.8	2	4.1
Total, 107	..	..	..	103	96.2	4	3.7
Inactive	43	..	..	27	62.7	16	37.2
	..	14	..	10	71.4	4	28.5
	..	..	2	2	100.0	0	0.0
Total, 59	..	..	..	39	66.1	20	33.8

In general, it will be noted that the greater the amount of lung involvement the greater the percentage of positive reactions, both in the active and inactive infections, and while it may be objected that the number of cases tested is small, I believe that further research will confirm these results.

Results of the Test in Group 2. This group, as stated, included all cases in which the clinical diagnosis was of some disease other than tuberculosis. In all, 250 individuals were tested, of whom 150 were suffering from syphilis and 100 from other diseases, including both acute and chronic conditions.

Of the total number examined, two gave a positive reaction with the test, or 0.8 of 1 per cent. In both positive cases the patients were syphilitic and gave a positive Wassermann reaction; but careful examination revealed lesions of the lungs suggestive of tuberculosis, although no bacilli were demonstrated in the sputum.

That the positive reactions obtained in these two cases giving a positive Wassermann reaction were not due to the syphilitic infection is proved by the fact that of 150 syphilitics tested, all giving a positive Wassermann, not one gave a positive reaction with the antigen employed in the complement-fixation test for tuberculosis here described, a result strongly in contrast with that obtained when Besredka's antigen is used, for with the latter antigen Bronfenbrenner obtained nearly 24 per cent. of positive results in syphilitics in whom tuberculosis was not suspected. He states, however, that 5 of the cases included in this percentage have since developed symptoms of tuberculosis, which reduces the percentage of positive results in syphilis to 17 per cent.

Of the patients suffering from other diseases, 100 in number, all gave a negative reaction with the test described in this paper, and while the number of cases is comparatively small, their great variety and the uniformly negative results obtained demonstrate, I believe, that this test will not react positively with diseases other than tuberculosis, nor with the blood serum in cases where a tuberculous infection has become encapsulated, for among this number of individuals there must have been many who had encapsulated tuberculous lesions and who would have given a positive reaction with the tuberculin tests.

Results in Group 3. The blood serum of 150 individuals in good health and free from tuberculous infection, so far as could be ascertained, was tested and a negative result was obtained in every instance. While these tests were made upon young, healthy soldiers, I am very sure that had any of the tuberculin tests been applied to the same individuals a considerable proportion of positive results would have been obtained if our conceptions regarding the percentage of individuals who have inactive tuberculous lesions are correct. The fact that the complement-fixation test in so many individuals was negative, speaks strongly in favor of its being a specific test for active tuberculous infection, and indicates that it will not give positive reactions in inactive cases or where the lesions have become encapsulated.

Discussion of Results. I believe that the experiments recorded in this contribution indicate that a complement-fixation test for tuberculosis, capable of giving as good results in the diagnosis and the control of the treatment of the disease as does the Wassermann test in syphilis, can be evolved, and that the test here described approaches very nearly this ideal. While it is unfortunate that so few cases of tuberculosis in the incipient stage could be tested, for it is in this stage of the disease that the test would be of greatest value in diagnosis, the fact that 60 per cent. of the cases that were tested in the incipient stage gave a positive reaction, although all were recorded as inactive clinically, speaks eloquently for the accuracy of the test in the diagnosis of early cases.

The results of the test also demonstrate that while a patient may have a clinically inactive tuberculous infection, the blood often gives a positive complement-fixation reaction, and this fact should prove of considerable value in the control of the treatment of the disease. While it would be premature to argue that a negative complement-fixation reaction in clinically inactive cases of tuberculosis means that the infection is cured, it is quite evident that in many cases proved to be inactive clinically a positive reaction *is* obtained, and this certainly would appear to indicate that there is still an active focus present, although no symptoms can be detected. On the other hand, where a negative reaction is repeatedly obtained and no symptoms indicating the presence of an active infection are present, it would appear to be reasonable to conclude that the infection has disappeared. However this may be, I am forced to conclude, as the result of these experiments, that a positive result with the complement-fixation test described, indicates the presence of an active tuberculous infection, even though the disease may be clinically inactive, and that as long as the test remains positive the patient cannot be said to be cured. This conclusion is based upon the uniformly negative results of the test in healthy individuals, the large percentage of positive results obtained in active tuberculosis, and the comparatively large percentage of positive results in clinically inactive cases of the disease.

The strength of the reaction has been found to vary from day to day in some cases, a strongly positive reaction alternating with a plus-minus or even a negative reaction. This variation in the strength of the reaction I have shown to[10] be true of the complement-fixation test in syphilis; and more recently, Irons and Nicolls[11] have shown the same to be true of complement-fixation in gonorrheal infections. Therefore, in this test, as in complement-fixation in the other diseases mentioned, a single negative reaction is of no value in excluding infection. Repeated tests should be made in all cases in which tuberculosis is suspected, and a negative report should not be made until several tests have been performed.

Conclusions. The following conclusions appear to be justified from the results of the complement-fixation test for tuberculosis reported in this paper:

1. Complement-binding antibodies are present in the blood serum of both active and clinically inactive tuberculous infections.
2. A polyvalent antigen prepared from several strains of the human tubercle bacillus has been found to give excellent results in complement-fixation for tuberculosis.
3. With the test described, complement-fixation gave a positive reaction in 96.2 per cent. of cases of active tuberculosis and in 66.1 per cent. of the cases of clinically inactive tuberculosis.
4. The test was negative in normal individuals and in patients suffering from other diseases with the exception of two patients infected with syphilis in whom symptoms of a coincident tuberculous infection was also present.
5. The test does not give positive results with the blood serum of syphilitics in whom there is no coincident tuberculous infection.
6. The reaction, when positive, is specific and apparently indicates.

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[10] Craig, C. F., Jour. Amer. Med. Assn., 1914, lxii, 1232.

[11] Jour. Infect. Dis., 1915, xvi, 303.

the presence of an active tuberculous focus, although there may be no symptoms of the disease present.

7. Positive results are obtained in a large percentage (66 per cent.) of clinically inactive cases of pulmonary tuberculosis, and such a result indicates that though it may be quiescent the infection has not disappeared.

8. The results obtained with the test described are practically as good as those obtained with the Wassermann test for syphilis.

Of course, much more work is needed before this, or any other method of diagnosing tuberculosis by complement-fixation is placed upon a thoroughly practical basis and is generally accepted as a routine diagnostic measure, but it is confidently believed that continued work upon this subject will result eventually in the perfection of a test that will be fully as useful in the diagnosis and control of the treatment of tuberculosis as is the Wassermann test in syphilis.

I desire here to express my thanks to Doctor Edward R. Baldwin for seven strains of the human tubercle bacillus kindly furnished me from the Saranac Lake Laboratory, and to Dr. Simon Flexner for three strains of the bacillus from the Rockefeller Institute. The antigens used in my experiments were prepared from six of the strains furnished by Dr. Baldwin and one of the strains furnished by Dr. Flexner.

LANDRY'S PARALYSIS: REPORT OF A CASE WITH NECROPSY AND HISTOPATHOLOGICAL FINDINGS.[1]

By Edward D. Fisher, M.D.,
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Many cases have been reported since Landry first described a disease characterized by a rapidly ascending paralysis passing from the lower to the upper extremities, thence to the cranial nerves, causing various paralyses, and ending fatally in the course of six or seven days with involvement of the vagus and respiratory failure. The pathological changes in the early cases were negative. This may have been due to the insufficient method of examination in part, but even in later reports very few changes have been found at times.

In the literature of this subject, which is considerable since Landry, in 1859, described his case, we find various lesions recorded in which either polyneuritis or spinal cord or bulbar inflammatory involvement has been present, or all in combination. Leyden and

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[1] Read before the Americal Neurological Society, New York City, May 8, 1915.

Goldscheider are among those who support this view. The cord changes are usually hyperemia, perivascular and pericellular infiltration, and hemorrhages into the gray and white matter; at times an interstitial and parenchymatous neuritis with or without cell involvement in the cord and bulb. The latter type is rather the exception than the rule. Our case belongs to the neuritic type with involvement of cells of the cord and brain stem.

E. Lugaro made an exhaustive study of reported cases of Landry's paralysis of the neuritic type up to 1904. He prefers to designate Landry's paralysis as a clinical entity characterized by an acute ascending flaccid paralysis, irrespective of pathological findings. And he cites cases of a purely neuritic type of Centanni, Eisenlohr, Leyden, Thomas, Reusz, Krewer, Wochenius, Roth, Rosenheim, Nauwerk, and Barth. All of their cases presented the same syndrome, namely, an acute ascending flaccid paralysis. Besides the interstitial and parenchymatous neuritis, there were also cell changes in the anterior and posterior horns of the cord. But these were of a reactionary type, due to remote influences in their neuraxones.

All authors agree that the disease is of infectious origin, and attempts have been made to isolate a specific organism, but without success. Centanni isolated a bacillus from the nerve trunks, Eisenlohr a Staphylococcus pyogenes and a Staphylococcus cereus albus from the spleen and sciatic nerve. Leyden's case came on after influenza. Wochenius found a Staphylococcus pyogenes albus in the spleen and peripheral nerves. In some cases pulmonary tuberculosis was a complication. Lugaro goes so far as to classify the cases reported by Korsakow and Serbski as puerperal polyneuritis, and similar ones reported by Prybitkow and one by Mader, as Landry's paralysis, because of the clinical picture.

Because of the fact that there is no specific agent causing the affection, he is inclined to advance the hypothesis that the toxin alone is responsible for the extensive destructive changes in the nerve tissues, and that in some cases only both the virus and its toxin are at work. He also points out that the time element as to the duration of the disease is not material for it may last a few days or a few weeks.

Since 1904 several other cases were reported that approximate my case both as to clinical and pathological data. Among them Pfeiffer, Burghart, Mosny and Moutier, and others report such types. The cases of Burghart and of Mosny and Moutier were complicated by pulmonary tuberculosis and lasted four weeks and two months respectively. In none of these cases was any germ isolated. Levaditti has injected a monkey with the emulsion of the cord of Moutier's case, and obtained negative results.

The case I shall record may be of interest, as it was observed from the onset, and a careful postmortem examination has been made.

Case Report. W. E., boy, aged fifteen years. Family history is negative. With the exception that he was operated upon for an inguinal hernia two years before his present illness, his personal history is negative.

Present Illness. September 27, 1913, he complained of a sharp pain in the calf of the left leg. This pain was gone the next day, but left him with a weakness in both lower extremities. He was able to walk without much difficulty but favored his left leg, holding it somewhat bent to keep him from falling. This condition grew progressively worse until October 11, when he was admitted to St. Vincent's Hospital, in the service of Dr. Constantine J. MacGuire. His paraplegia was then complete and he had to be carried to the hospital.

Status on Admission to the Hospital. Patient was well developed and a little above the average height for his age. The temperature was 99.2°, pulse 72, and respirations 24.

Examination of heart, lungs, and abdominal viscera was negative.

Muscles of the head and neck and of upper extremities were normally active. There was a flaccid paralysis of the lower extremities, with loss of reflexes and pain on pressure over the large nerve trunks. There was no dissociation of touch, pain, or temperature sense. No anesthesia. Deep muscle sense was normal.

Laboratory Findings. Urine, amber color; acid; specific gravity, 1019; albumin and glucose negative; no casts; no crystals. Blood: leukocytes, 23,500 per cubic millimeter; polynuclears, 86 per cent.; transitionals, 2 per cent.; lymphocytes, 12 per cent. Spinal fluid clear and colorless; normal pressure. Fehling's reduction test positive; globulin slightly increased and 7 cells per cubic millimeter. Smears and cultures negative for bacteria. Wassermann reaction negative in blood serum and spinal fluid. Throat cultures negative.

October 15. Patient vomited and complained of severe abdominal pain and chilly sensations. Blood culture taken and proved negative. The pain and vomiting were relieved by catharsis and colonic irrigation.

October 17. Complains of seeing double and holds the left eye closed so as to prevent it. Paralysis of left external rectus. Dr. Kelly examined the eye-grounds and found them to be negative.

October 25. Restless the greater part of the night and complains of pain in the left shoulder. Has a headache and vertigo and vomited after lunch. From this time he had a progressive weakness and loss of power in arms and hands, until in about one week it was complete.

October 29. Headache is gone, but complains for the first time of some difficulty in swallowing. Dr. Kelly reports now complete paralysis of the muscles of the right eye and of the superior oblique of the left.

November 1. Blood count: leukocytes, 5900; polynuclears, 60 per cent.; lymphocytes, 38 per cent.; basophiles, 2 per cent.

November 3. Complains of pain in the cardiac region.

November 9. Again had difficulty in swallowing, and had pain in the back and temporary shortness of breath.

Neurological Examination. Cranial nerves: I, unaffected; II, negative; III, left normal; almost complete right-sided palsy; right ptosis; pupils react to light and accommodation well; IV, left paralyzed; V, right affected; diminished sensation of cornea and right side of face; weakness of masseter; VI, left paralyzed; VII, bilateral facial paralysis of the peripheral type; unable to wrinkle forehead, show teeth or close eyes tightly; difficulty in pronouncing consonants "b" and "p"; VIII, IX, and X, normal; XI, affected; trapezii and sternomastoids weakened; XII, normal. Motor functions: double foot-drop with complete loss of power in legs, flexors, and extensors being equally involved. Double wrist-drop. With the exception of slight movements of fingers, almost complete paralysis of upper extremities. Muscles of trunk markedly involved.

Sensory functions: Coördination, deep muscle sense normal. Decreased touch and temperature sense.

Trophic disturbances: Marked atrophy of muscles of lower extremities. Slight atrophy of muscles of arms and hands.

Reflexes: K. J., A. K., W. K., E. K., absent. Abdominals present. Pupillary normal. Sphincters normal.

Electrical reactions: Absence of faradic response and R. D. present in lower, quantitative and qualitative diminution in upper extremities.

November 17. Marked shortness of breath, respirations 40, almost wholly costal. Pulse, 90. First valvular sound impure, second pulmonic accentuated. Pulmotor had to be used to relieve dyspnea. Pulse went up to 150, and was weak and thready.

November 21. Patient died of respiratory failure.

Necropsy. Dr. John H. Larkin made the autopsy and reported that the thoracic and abdominal viscera were normal. The cord showed an intense congestion, but otherwise was macroscopically negative. Sections of the sciatic nerve, cord, medulla, and pons were prepared by him and studied by Dr. M. Neustaedter, who makes the following report on the histopathology of the case:

MICROSCOPIC STUDY. Sections of all levels of cord, medulla, pons, and the sciatic nerve were examined. These were stained according to the methods of Nissl: toluidin blue and polychrome methylene blue; Van Gieson, Mallory, Bielschowski, Weigert-Pal, Nigrosin stain; Marchi and Sudan III.

Spinal Cord. Sections from the lumbar, dorsal, and cervical segments. The cells of Clarke's column show a central chromatolysis, with remnants of small, narrow, and poorly defined and darkly staining bodies lining the periphery of the cells. The protoplasm of the remaining cell is a diffused granular mass assuming a faint stain and giving the cell a dusty appearance. The cells are markedly swollen, and nuclei, when present, are eccentrically situated. The nucleoli stain rather darkly and under high magnification show a disintegration of their substance into bodies of various shapes and sizes. The cell prolongations are everywhere faintly stained. This degeneration is manifested in all the cells of Clarke's column at all levels of the cord. Nowhere along this column is any evidence of a neuronophagocytosis to be found, although there is a fair amount of hyperplasia of glia cells in their vicinity.

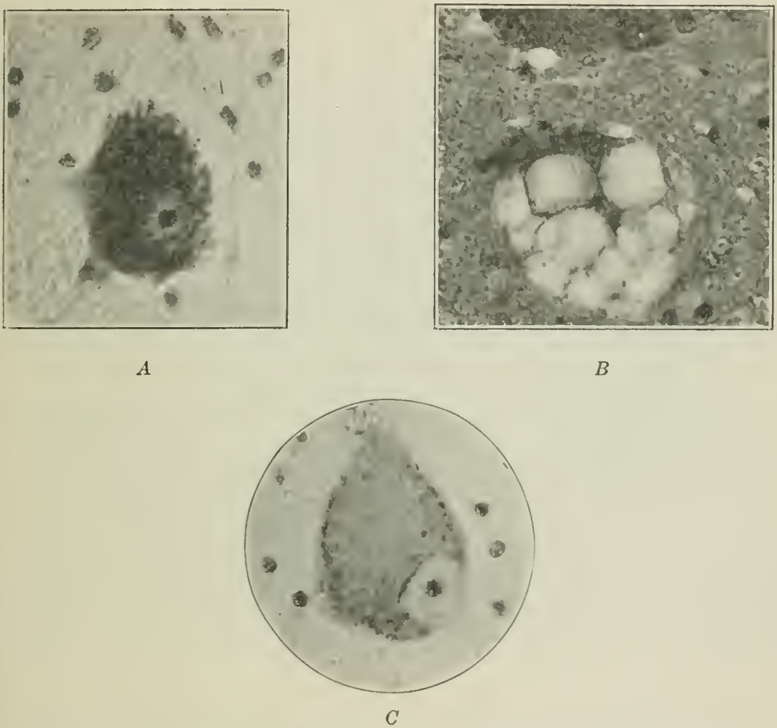

Fig. 1.—*A*, degeneration of anterior horn cells, showing a tygriosis and a beginning chromatolysis around the periphery, with eccentric nucleus. Nissl stain. Zeiss, 8 mm. Oc. 6. × 450. *B*, cell vacuolization of anterior horn cell. Van Gieson stain. *C*, degeneration of cells of Clarke's column, with central chromatolysis, chromophilic substance lining the periphery. Nissl stain. Zeiss, 16 mm. Oc. 3. × 60.

The large multipolar cells of the anterior horns throughout all the segments of the cord are seen to have undergone three forms of degeneration of various intensities. The most prominent feature is a coalescence of the tygroid substance, a tygriosis, and a consequent shrinkage. The cells stain darkly or assume such an intense stain that the chromophilic substance cannot be differentiated at all. This condition cannot be an artifact or overstaining, since other cells on the same section are staining quite well. In assuming such a dark stain the cell obliterates the view of the nucleus if present. In some cells the nucleus is eccentric and its cytoplasm broken up into irregular bodies and the nucleolus is staining very deeply. The prolongations of these cells are visible and retain slight meshes of chromophilic substance. Around the periphery of the cells and at times dipping into the cell body itself are seen round cells, large and small, of the type of satellite cells. To a lesser extent we find cells in the anterior horns, with a central chromatolysis of the type described in the cells of Clarke's column. In cells affected by this phase of degeneration the prolongations are gone and no evidence of any neuronophagocytosis is present. Very rarely, indeed I have only seen it on three sections, there appears to be a cell vacuolization with the nucleus entirely gone and a slight neuronophagocytosis present. The first type of degeneration is most pronounced in the anterior horns of all the cervical and dorsal segments, while the second type is most pronounced in the anterior horns of all levels of the lumbar region and in the cells of the lateral horns all over the cord.

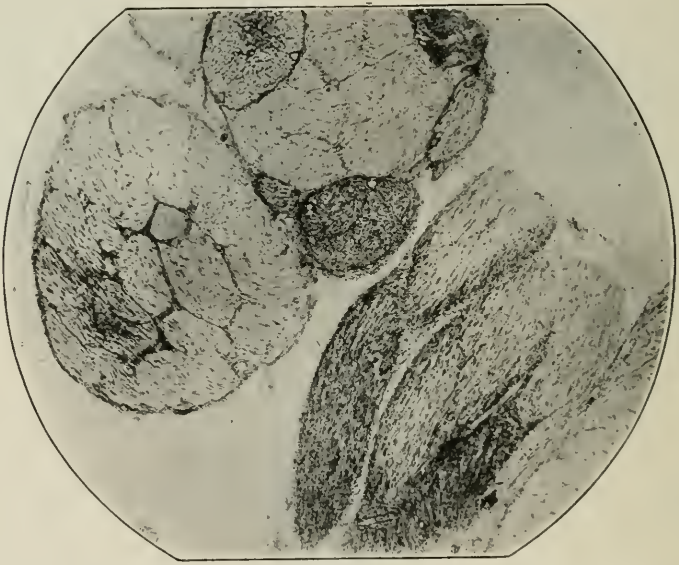

FIG. 2.—A diffuse and focal infiltration of leukocytes in the anterior nerve root, cervical segment. Nissl stain. Zeiss, 16 mm. Oc. 3. × 150.

The significance of these phases of cell degeneration has been established by pathological investigation and experimentation, namely, that a central chromatolysis with swelling and eccentricity of the nucleus, together with chromophilic substance present in well-defined meshes around the periphery of the cell, is accepted to be a reactionary degeneration or attempted regeneration of the cell as a result of a lesion remotely in the cell prolongation—in the neuraxone. While the degeneration beginning as a tygriosis, coalescence of the chromophilic substance accompanied by swelling in some instances, and a shrinkage or cell vacuolization following it in the presence of a more or less marked neuronophagocytosis and a gradual cell destruction in which the tygroid substance is present as long as a part of the cell is present is accepted as an inflammatory reaction within the cell itself, or its pericellular lymph space or in the substance of its immediate neighborhood. In the first type we see slight evidence of any remaining neuraxone or other cell prolongation, while in the latter type we always see a well-stained cell prolongation with some meshes of the chromophilic substances.

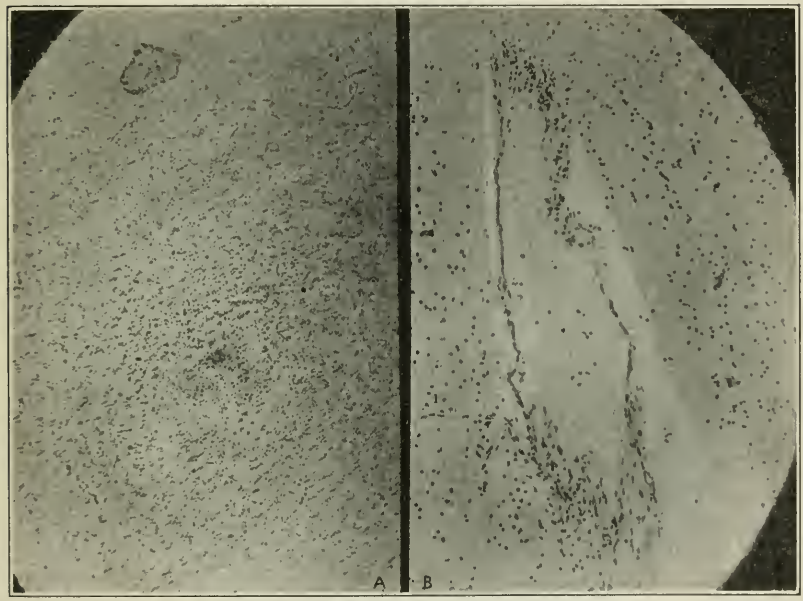

Fig. 3.—*A*, focus of marked glia-cell proliferation in the gray matter in the neighborhood of the aqueduct on a section through the red nuclei. Nissl stain. Zeiss, 16 mm. Oc. 3. × 60. *B*, slight perivascular infiltration of mononuclears in the same neighborhood. Nissl stain. Zeiss, same magnification as *A*.

In view of the fact that we have the first type of cell degeneration present to a great extent, and the second type only in some parts of the anterior horns, we should expect definite pathological changes in the peripheral nerves and a clinical picture in conformity with these. This discussion we shall leave to the end after first reporting the other findings.

Sections stained by the Bielschowski method show a marked degeneration of the neurofibrils of the cells of the anterior horn, while those of the cells of Clarke's column are entirely absent. This is true of all the levels of the cord.

There is a considerable hyperplasia of glia cells in the gray and white matter of the whole cord, and not infrequently do we meet with darkly staining, small mononuclear round cells, especially pronounced in the neighborhood of the blood vessels, filling in their perivascular sheaths to a very slight extent. They are most probably lymphocytes.

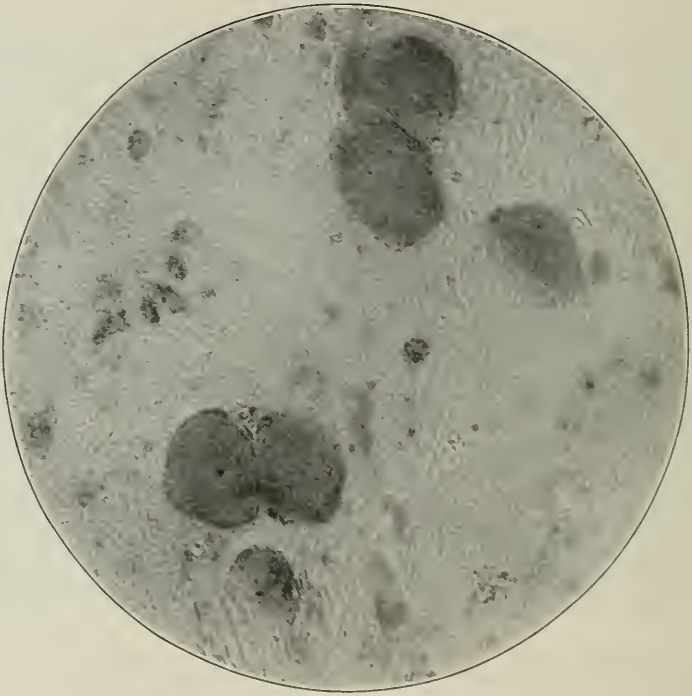

Fig. 4.—Swelling, central chromatolysis, and degeneration of the cells of the descending nucleus of the fifth. Nissl stain. Zeiss, 8 mm. Oc. 6. × 440.

A feature of considerable interest in this case is the ependymitis around the central canal, especially well established at the levels of the cervical and lumbar enlargements. We find here a considerable hyperplasia of ependymal cells with an intense infiltration of large polymorphonuclears around the central canal with not an inconsiderable amount of small, darkly staining mononuclears. At some levels of the cervical enlargement there are even some large polymorphonuclears found within the lumen of the canal.

Finally, it must be noted that the capillaries of the gray matter of the anterior horns are engorged. In many instances one notices capillary aneurysms, and not infrequently these burst and give rise to extensive hemorrhages. Hemorrhages of the white matter I have noticed only in a few instances in the posterior columns.

The Medulla and Pons. The cells of the nuclei graciles and cuneati show a pronounced degeneration of the type found in the cells in Clarke's column of the cord, while the cells of the motor nuclei and of the formatio reticularis show evidences of the type of degeneration we found in the ganglion cells of the anterior horns of the cord, namely, a tygriosis. Throughout the segment at the level of the decussation of the pyramids there is a fair amount of hyperplasia of glia cells and some diffuse and very slight perivascular infiltration of deeply staining, small, round mononuclears. The central canal shows here also some ependymitis as in the cord.

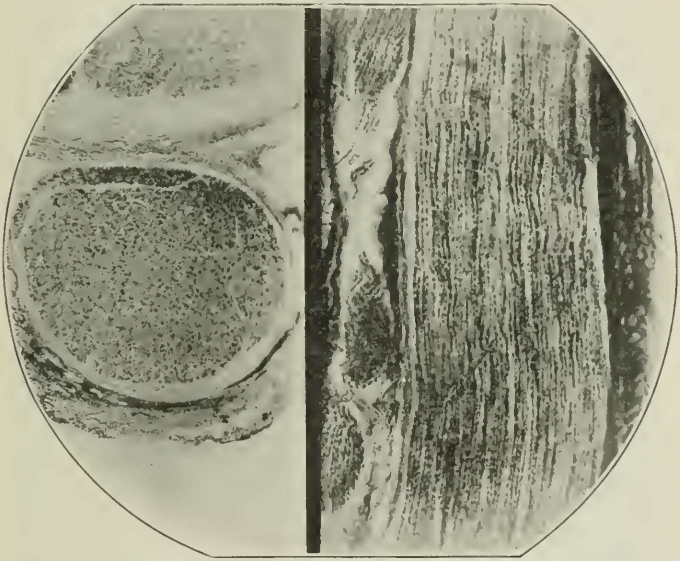

FIG. 5.—Longitudinal and cross-sections of the sciatic nerve, showing pronounced degeneration of the myelin substance. Marchi and Weigert-Pal stains. Zeiss, 16 mm. Oc. 3. × 60.

The cells of the nuclei of the third and sixth cranial nerves show the following form of degeneration. There is a central chromatolysis around the nucleus, which in most instances is at the periphery, while the tygroid substance of the remaining cell has undergone disintegration, appearing in irregular, thick, and broken meshes. The nuclei are swollen and stain very lightly while the nucleolus assumes a dark stain. The cell prolongations are visible. Many of the cells are gone for the greater part and no trace of the nucleus would be present. The capillaries are filled and in some instances there are thrombi present. These changes are also evident in the sensory nucleus of the fifth and the sensory as well as the dorsal nuclei of the tenth nerves. The nucleus ambiguus shows no change that I would consider pathological. The cells of the descending and ascending roots of the fifth are very much swollen and show a general chromatolysis with the protoplasm disintegrated into a fine granular mass giving the cell a peculiar dusty appearance. At the periphery there are still evident darkly staining tygroid bodies, and their neuclei when present are eccentric and swollen, staining very lightly with the nucleolus staining somewhat deeper. The cell prolongations of these cells are totally gone and there is no evidence of any peri-

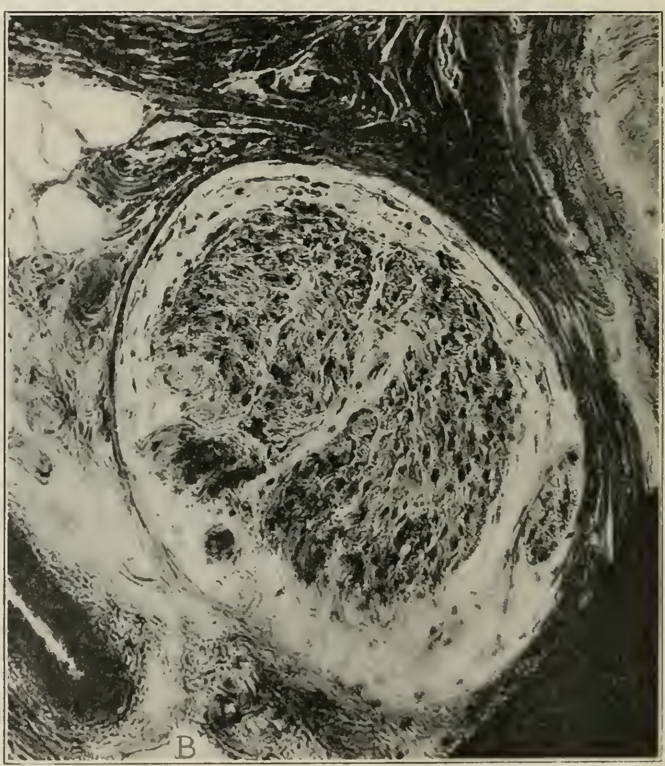

Fig. 6.—Cross-section of sciatic nerve, showing proliferation of the perineurium, extensive parochymatous degeneration of nerve fibers, and connective-tissue increase; infiltration of leukocytes and Gitter cells. Some thickening of the endoneurium and fatty degeneration of the perineurium. Mallory stain. Zeiss, 8 mm. Oc. 6. × 250.

cellular infiltration. The cells of the nuclei of the seventh and twelfth nerves show changes characteristic of the motor nuclei of the bulb at the level of the decussation of the pyramids. In the cells of the other pontine nuclei, the nuclei rubri, and basal ganglia show alterations similar in type to those of third. In the region of the nucleus ruber we find also some perivascular infiltration of mononuclears and endothelials, and also some focal infiltration of small, darkly staining mononuclears and polymorphonuclears as well as some hemorrhages. The glia cell proliferation is very much marked throughout.

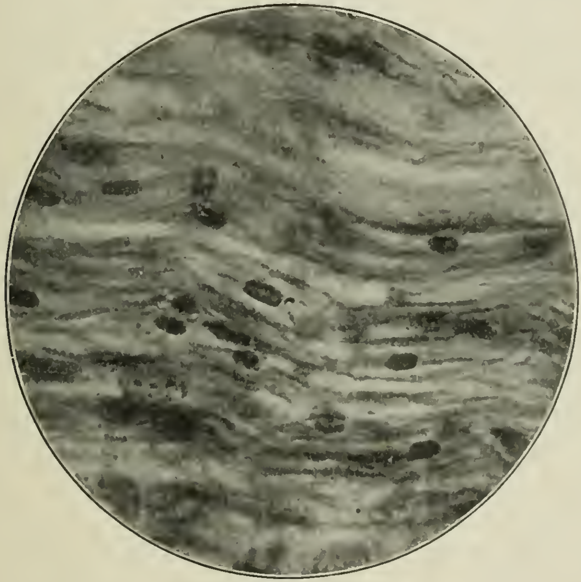

Fig. 7.—Posterior nerve root, lumbar segment showing polyblasts and some Gitter cells. Mallory stain. Zeiss, 8 mm. Oc. 6. × 400.

The spinal nerve roots of all segments stained by the Nissl method show at times a diffuse and at times a focal-cell infiltration into the lymph spaces of the epi-, peri-, and endoneurium. Those of the lumbar segments are most intensely affected. The anterior roots are far more involved than the posterior. This infiltration is not only evident in the distal end of the nerve trunks but also at the entrance of the nerve roots, and which consists of small, round, darkly staining mononuclears, fat granular cells, and polyblasts from which the latter are really formed. At times there is to be seen a hemorrhage into the posterior nerve root, the contiguous white substance of the cord, and into the pia. The thoracic segments are subjected to this change. There is also an infiltration of the perivascular lymph spaces at the nerve roots which consists of mononuclears and endothelials. The cross-sections of the anterior and posterior nerve roots stained according to methods of Marchi, Mallory, Van Gieson, Bielschowski, and the Nigrosin stain show markedly destructive parenchymatous and interstitial changes. It would seem that the toxic substance has been propagated through the perineural lymph spaces in a comparatively rapid time, producing such extensive and destructive changes. In other places we find a complete breaking down of all the elements of the nerve fiber, a thickening of the endoneurium, and a proliferation of the connective tissue.

The peripheral nerve studied is the sciatic. With the polychrome blue stain there is evident an infiltration of cells, but not as marked in the nerve roots. This infiltration is mainly pronounced in the peri- and endoneurium, and consists of polymorphonuclears, polyblasts, and Gitter cells. Here and there one finds a lymphocyte. The infiltration is most marked in the neighborhood of bloodvessels. There is also a slight proliferation of cellular elements, but their protoplasmic processes are not visible. The connective-tissue and endothelial cells are more proliferated than other cell elements. Especially on cross-section one observes a very marked connective-tissue cell proliferation with their protoplasmic processes extending to some extent between the nerve fibers. The Schwann cells are rather swollen. With the Marchi stain there is to be noted a degeneration of the myelin substance, forming irregular masses scattered throughout the nerve fiber. With the Van Gieson and Nigrosin stains a very extensive nerve fiber destruction is to be seen. The peri- and endoneurium appear markedly thickened, their vessels show a considerable infiltration into their lymph spaces, consisting of large and small round cells. Their endothelial coat is thickened and the endothelium loose. The proliferation of connective-tissue fibers and cells is quite evident. There is also a pronounced infiltration of polyblasts and Koernchenzelln among the fibers. The Schwann nuclei are swollen and stain deeply, and at times fairly occlude the lumen of the fiber. Some fibers show an obliteration of the axis-cylinder, and the myelin substance presenting masses filled with fine, dusty granules assuming a bluish tint with the nigrosin stain. Others, again, show no differentiating characteristics at all, but become confluent into a connective-tissue mass with a marked cell infiltration.

In view of such extensive parenchymatous and interstitial changes in the nerve roots and trunks the question comes up whether we are dealing with end results of a toxin or a bacterial activity, or of both. The cell infiltration would point to a bacterial invasion resulting in a phagocytosis along the lymph spaces of the nerves through which the virus was disseminated. In view of the fact, however, that the infiltration is not marked in all places alike, and in some instances it is rather slight, although the changes in the fibers are very pronounced, and in view of the fact that the duration of the disease was rather longer than usual, I hold that both the virus and the toxin did play an equal part in bringing about these changes in the peripheral nerves primarily, and these gave rise to the reactionary cell changes in the cord and medulla and pons. The ganglion cell changes, however, which are accompanied by a slight neuronophagocytosis are, in my opinion, the direct result of the virus.

CONCLUSION. We have here, therefore, a case of ascending paralysis, with attending neuritis, which followed the usual course of extension, later involving the upper extremities and bulbar nerves resulting in respiratory failure. The pathologic findings are definite, involving both the peripheral and central nervous systems. The course of the disease was longer than usually described, extending over six weeks, but otherwise the case was typical in its clinical manifestations.

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THE VALUE OF SYMPTOMATIC DRUG TREATMENT.

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As compared with a few decades ago, drug therapy occupies a less prominent place in the treatment of disease, and inasmuch as most of our medication is symptomatic in character, it probably means that symptoms are less frequently treated than in former years. Is this to be considered a step in advance, or are we, on account of our interest in scientific medicine, negligent of an important detail in treatment? It is probably true that with the development of specific drug therapy and biological products the physician has become more impatient with and less interested in treatment directed toward giving only temporary relief. Other important reasons, however, must be considered. The profession each year contains more and more men with careful scientific training. This training may have led them to scrutinize more closely all methods of treatment through carefully controlled observations. The advance of pathological physiology, pharmacology, and experimental therapeutics has furnished them with certain knowledge, and especially a new method of applying it. As a result of all this there has developed, as it appears to the writer, a certain healthy skepticism in regard to drug therapeutics.

Certain points should be considered before undertaking any symptomatic treatment. A few that might be mentioned are: Should this particular symptom be corrected? Does it interfere or assist in bringing about improvement or recovery? Will its modification interfere with making a correct diagnosis or obscure observation upon the progress of the condition? Having determined that a certain symptom should be treated, it is necessary to determine, if possible, the underlying pathological physiology and then the agent to correct it. Not merely the chemical agent but the necessary dosage and frequency with which it should be repeated in order to bring about the desired effect. To attempt to lower blood-pressure, at least under certain conditions, may be poor therapeutics; as, for instance, when due to increased intracranial pressure, when the rise in blood-pressure is an effort to avoid cerebral anemia. It is not improbable that hypertension of renal origin is an effort to increase the efficiency of a pathological kidney. Drug antipyretics, on account of their depressing action, have been largely abandoned in the treatment of prolonged fever. The recent investigation of Rolly and Meltzer and Ludke and others raises the question whether any method of artificially lowering temperature is desirable, as according to their experiments at least a certain degree of fever favors the development of immune bodies. Before undertaking symptomatic treatment it is wise to consider the compensatory resources of the body and not confuse compensatory action with what is commonly regarded as a disease symptom.

In the severe acute infection if we decided the centres in the medulla are not functioning properly can we modify them by certain drugs? We are taught by the pharmacologists that strychnin quickens and deepens the respirations and stimulates the vasomotor centre, causing slowing of the pulse and a rise in blood-pressure. Now if these same results were produced at the bedside upon these centres, rendered abnormal by toxins, we would have in strychnin a valuable symptomatic remedy. Whether under the conditions mentioned, and in the usual doses, strychnin stimulates these centres sufficiently to bring about any appreciable improvement is exceedingly doubtful, as shown by the observations of Cabot, Newburgh, and others. We must therefore conclude that either our conception of the pathological physiology is incorrect, and the recent work of Newburgh indicates that in this particular illustration this may be the case, or our pharmacology is at fault. Symptomatic treatment, however, when applied to the correction of undesirable symptoms by agents that have been demonstrated to correct this disturbance is strictly scientific, and in this respect is placed at once on the same level as specific therapy.

There is another group of conditions in which symptomatic treatment is not only strictly indicated but in which the agents are at hand to give relief. Morphin when administered to a pneumonia patient with acute pleurisy not only relieves the pain, but deepens the respiration, improves the oxygenation of the blood, promotes sleep, and thus becomes far-reaching in its results. In an acute attack of pulmonary edema, morphin is often of considerable value, in a measure due to its relieving the patient's fears and thus lowering the arterial blood-pressure, and so permit of a restoration of function of the left ventricle. Morphin in acute biliary or renal colic relieves pain, and at the same time relaxes muscular spasm, thus allowing the calculus to escape. Adrenalin, by relieving bronchial spasm, may abort an attack of bronchial asthma. Angina pectoris when due to spasm of the coronary artery may be relieved by the nitrites.

There is another group of conditions in which symptomatic treatment may give only transitory relief, but when combined with other agents may give prolonged relief. This form of symptomatic treatment can only be considered scientific when associated with these additional measures; as, for example, digitalis, although claimed as a functional remedy, is nevertheless, given to relieve symptoms, as, for instance, dyspnea. Alkalies are of value in relieving gastric hyperacidity. The digitalis, however, should be combined with restriction of physical exertion and the alkalies with the proper dietary measures in order to give lasting results.

Outside of the symptoms that can be placed in these groups mentioned or others of the same rational character, there is another group the treatment of which at least today cannot be considered as proved rational therapy. Here might be included the value of salicylates in acute arthritis, of expectorants, of bitter tonics, of arsenic in anemia, and of drugs used to control hemorrhage. It is in this field that the clinical therapeutist can render real service. Here a process of elimination is necessary in order to place therapeutics upon the same high plane as the other branches of medicine.

In addition there is a long list of drugs employed symptomatically proven to be without value, mentioned or recommended still in modern high class text-books. As an example we might name hexamethylenamin, which rapidly acquired a reputation as having bactericidal properties throughout the body and when administered by mouth to appear in the form of formalin in the various excretions and secretions of the body. It is still extensively used in respiratory and ear infections, in meningitis, arthritis, and cholecystitis; although it has been clearly demonstrated that the hexamethylenamin is only split up and formalin set free in an acid media and of the various secretions, the urine is the only one which is acid.

In order to determine the value of symptomatic treatment it is very essential that the observer be familiar with the course of untreated disease. Individual variations must always be taken into consideration. Many patients with pernicious anemia grow progressively worse, others have prolonged periods of spontaneous improvement, the latter offering a dangerous pitfall for the unwary therapeutist. Perhaps in the teaching of clinical therapeutics it would be wise to instruct the student first in the course of untreated disease; if possible to follow a few cases in the ward, tabulating symptoms, their intensity and duration. He would thus be impressed with the importance of carefully recording symptoms. He would thus be in a better position to determine the effect of therapeutic agents, and so avoid the error of acquiring experience in clinical therapeutics in a haphazard and time-consuming manner. For the purpose of arriving at accurate information too much stress cannot be laid upon the statistical method of which Dr. Osler has always been a strong advocate. While the impression of our therapeutic accomplishments may be more pleasant to consider, it is carefully collected and recorded information that is of lasting benefit to medicine. Our therapeutics can be placed upon the same accurate basis as pathology and symptomatology. Symptomatic treatment is most important not only from the stand-point of the patients, but also for the purpose of clearing up the field of clinical therapeutics, and he who undertakes a careful study of symptomatic therapeutics will be rendering a lasting service to medicine.

THE PROBLEMS OF NEPHRITIS FROM THE CLINICAL STAND-POINT.

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Until a comparatively recent period our knowledge of nephritis was mainly accumulated by the methods of clinical observation and anatomical research. Clinical study has slowly and laboriously amplified in matters of detail the essential facts contained in Bright's original conception of the clinical pathology of kidney disease, but has failed to alter or in any important degree to add to the fundamental principles outlined by the founder of renal pathology. The study of the morbid anatomy of kidney disease with resulting attempts to form classifications based thereon begun by Frerich in 1851 still continues, although latterly with less enthusiasm for such elaborate classification as characterized pathological research in ultrascientific circles twenty years ago. This decline in the vogue of pathological classification followed inevitably the too great intricacy of many of the classifications and their frequent failure to correlate satisfactorily with clinical manifestations and urinary signs, resulting in division and subdivision beyond the point where the various types can be recognized clinically. With the realization that the methods of pathological study alone offer little prospect of an interpretation of many important aspects of renal pathology, investigation has turned to the study of nephritis in animals produced by experimental technic. Such investigations appear to lend themselves ideally to this purpose, since they include studies in function as well as morphology, thereby overcoming, partially at least, one of the serious shortcomings of purely histological research. These studies in experimental nephritis, actively prosecuted for a period of ten years, while they have added greatly to our knowledge concerning the function of individual parts of the kidney and the way these functions are disturbed in lesions of different kinds, have as yet failed to elucidate important points in pathogenesis. The effect to this point, of the experimental investigation of kidney problems, upon the clinician has been to add to the difficulties of an inherently difficult subject. Enough has been done to indicate that many former beliefs were erroneous; old convictions have been unsettled without the substitution always of definite and reliable information. This inevitably marks the middle stage of any investigation, and need not shake our faith that experimental investigation will finally solve the many important problems concerned.

Coincidently with and largely as an outcome of these activities in research aspects of nephritis the progress of science has introduced new factors into the clinical outlook that afford us valuable aid in the examination of nephritis patients and materially assist us in our attempts to secure a good basis for diagnosis, prognosis, and treatment. Advances in our understanding of chronic infective processes and their relation to systemic disease, the introduction of the blood-pressure gauge into general practice, a more scientific procedure in dietotherapy, and the perfection of tests for kidney function combine to render clinical procedure much more exact and scientific than formerly. It is now no longer enough to state that the patient has acute or chronic nephritis. The diagnosis must be completed with an attempt to elucidate its cause, with an adequate study of the circulation, with an estimation of total renal function, and if we strive to be exact, with a further specification as to whether there is retention of chlorides or nitrogen. Modern procedures enable each of the above factors to be studied. It is with the bearing on clinical considerations of these newer aspects of the nephritis problem that the present discussion is concerned.

The problem of acute nephritis is essentially different from that of chronic nephritis. In acute nephritis we have to do with acute damage to normally functioning organs which, previously sound, are again more or less quickly restored to normal provided they are not overwhelmed by the destructive agent. In the chronic nephropathies it is the possibilities for the establishment of compensation that constitute the problem. The etiology of acute and subacute nephritis may be said to be invariably either bacteria or their toxins, and of the bacteria concerned, by all means the most important is the streptococcus. This intimate connection between sepsis and nephritis has been frequently mentioned in literature since Bartels first noted it in 1877, but the full extent of the role played by bacteria has hardly had sufficient appreciation. Acute nephritis is usually due to the action of bacterial toxins, the renal reaction being a diffuse inflammatory affair. More rarely nephritis may result from actual lodgement of bacteria in the kidney substance (bacterial thrombi), when cocci may appear in the urine, giving rise in consequence to a disseminated focal type of lesion, of which a good example is the embolic glomerulonephritis of subacute bacterial endocarditis. The existence of acute nephritis (excepting, of course, the rare chemical nephritides) invariably points to a pre-occurring infection. In seventeen cases of acute and subacute nephritis studied by Ophüls,[1] all were found to be suffering from septic processes. The importance of identifying the original source of the sepsis is great, for upon its detection and removal depend, during the earlier stages at least, success in controlling the renal secondary. The tendency of uncomplicated acute nephritis is to recovery, provided infective factors be no longer present and active to work new damage to the kidneys. This is well shown in clinical experience, on the one hand, by the complete disappearance of the nephritis of scarlet fever in those cases that survive, and, on the other hand, by the marked tendency to chronicity that characterizes nephritis associated with tonsillitis, owing to the frequent persistence of focal infection in the tonsil. As illustrating the latter point may be mentioned a recent case where a subacute hemorrhagic nephritis of four months' duration in a child, aged ten years, disappeared within three weeks following radical removal of infected tonsils.

In the matter of chronic nephritis the problem of etiology is much more difficult. The material has been worked over by generations of pathologists, and yet the etiology of most cases is entirely obscure. No doubt in a certain proportion of cases a history of acute nephritis may be elicited, but the connection between the two is not always clear. There is one difficulty that presents itself from the clinical side in investigating the question of the connection between acute and chronic nephritis, and that is that acute and subacute nephritis may occur without the development of symptoms, other than the urinary signs, during any infection, and failure to analyze the urine may sacrifice the opportunity to discover the original first link in the chain that perhaps leads to a final chronic nephritis. In consequence of this it is difficult, if not impossible, to exclude an antecedent acute nephritis in any given case. Considering the nature of chronic renal disease and what we know of the action of chronic focal or confined infection (sepsis), it would appear likely that certain types of chronic nephritis follow less frequently single acute renal inflammation than that they eventuate from repeated subacute inflammatory reactions consequent upon rise and fall in the activity of chronic septic foci such as exist in infected tonsils sinuses, etc. I have recently observed three distinct attacks of subacute nephritis, with pus in both maxillary antra, in a young man, during the space of one year. Drainage of the antra resulted in prompt disappearance of this renal secondary. Müller expresses the opinion that a chronic nephritis may be the result of an acute lesion with a progressive course marked by acute exacerbations. Our present understanding of infective secondaries would indicate that a progressive exacerbative acute nephritis is the product of a persisting infection or of recurring acute infections. This is the type of chronic kidney met with in association with chronic focal or confined infection (sepsis). Experimenters have found that acute nephritis induced artificially rapidly disappears and that the kidney returns to normal. This is in keeping with the well-known clinical observation that an acute nephritis if its causative agent be no longer operative usually goes on to healing without the development of subacute or chronic lesions. Many cases of chronic nephritis apparently following the acute lesions of scarlet fever have been reported, and both Müller and Löhlein describe a type of chronic nephritis developing several years after acute lesions of scarlet fever and coccus infections, the inflammatory glomerular changes of the primary acute nephritis apparently serving as the starting-point for later fibrotic and indurative lesions. Whether a certain number of these chronic lesions are not spontaneous in origin appears a fair question. The experimental study of nephritis in the main supports the more common conception of the etiology of chronic nephritis in man—that it is a gradually developing lesion due to the long-continued insidious action of some ill-defined toxic substances (Pearce[2]). When we consider what these toxins are, very little clear information is available. Apart from the subacute and chronic inflammatory types of nephritis in which chronic sepsis, including syphilis, can be identified or clearly inferred, we are at present ignorant of the ultimate cause of chronic nephritis aside from the well-known ability of chronic lead intoxication to cause progressive kidney lesions. Recently an increasing importance is being attached to the etiological role of circumscribed and confined infection commonly called focal infection, and it is assumed that it may prove to be an important factor in the production of chronic nephritis. That it may play a first-class role in the causation of subacute and chronic inflammatory nephritis is already fully recognized, but the connection between such a factor and the vascular nephropathies (contracted kidney), while possible, remains for investigation and observation to prove. A certain percentage of cases of this class belong to the type known as secondary contracted kidney. This is the terminal atrophy of acute inflammatory reactions, and as such has a more or less remote connection with acute nephritis, although the original infection or sepsis may have long since ceased to operate as an etiological factor. The tendency of acute nephritis when it becomes chronic is toward either epithelial degeneration or interstitial fibrosis. Epithelial degeneration eventuates in the large white kidney ("parenchymatous nephritis"), whereas the fibrotic organ becomes the so-called secondary contracted kidney. Herringham emphasizes the fact that these are not consequent the one on the other, and he thinks much of the confusion existing arises from regarding them as sequential. Each is individually a terminal development of what was primarily the same acute process. Herringham employs an excellent illustration to define this divergence by citing the development of pulmonary tuberculosis which in one case proceeds by a continuously spreading bronchopneumonia, with softening and cavity formation, while in a second case the tendency is markedly toward fibrosis. In somewhat similar manner typical cases of diffuse nephritis in full development may differ so widely both in clinical symptoms and pathological appearances that they might be two separate diseases. There is, however, no greater difference in these two terminations of acute nephritis than there is in the two forms of phthisis, one a caseating tuberculous bronchopneumonia and the other fibroid phthisis. It has generally been assumed that secondary contracted kidney is uncommon, and the older authorities looked upon it as a great rarity. We are beginning now to understand that it is comparatively frequent, principally owing to the work of Löhlein. He succeeded in collecting quite a number of cases that clinically as well as anatomically were evident examples of this type, and he pointed out that on account of the comparative ease with which he discovered such cases they cannot be as rare as was formerly believed. In Ophüls' series the so-called secondary contracted kidney was responsible for 11 out of 37 cases of seriously contracted kidney, a percentage that furnishes a startling indication of its frequency.

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[1] Arch. Int. Med., 1912, ix, 156.

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[2] Arch. Int. Med., 1910, v, 133.

From the clinical stand-point it is not surprising that these cases are seldom differentiated. There are no absolute and reliable symptomatic criteria that suffice to identify them. In those cases where a clear history of acute nephritis exists, and no doubt intrudes that it was a genuine acute nephritis and not an acute exacerbation of a chronic although perhaps latent lesion, the assumption may be reasonably plain that the secondary contracted kidney exists. Anyone who has looked into the question will recognize that the cases of contracted kidney that give a history of an acute beginning are a small minority. Far the greater number begin insidiously with no severe symptoms. They are either discovered accidentally or an acute exacerbation supervenes which is at first thought to be a primary acute attack until careful inquiry or subsequent observation makes it certain that nephritis has existed for a long time. The secondary contracted kidney in its clinical manifestations closely resembles primary contracted or what is generally known as chronic interstitial nephritis. Such differences as exist are in degree rather than in kind. The clinical picture is perhaps more frequently dominated by a glomerular oliguria, although if a sufficiently large part of the filter apparatus is spared there may be polyuria for the same reason as in primary contracted kidney. As Aschoff[3] points out, the primary factor at work being an inflammatory change affecting the filter apparatus itself (glomerulonephritis), the organ is placed under a more serious handicap as to filtration area than is usually the case in primary contracted kidney. In consequence of this, function is maintained with difficulty, the organs working constantly on the borderline of their maximal capacity. The course of the disease is apt to be characterized by a delicacy of functional adjustment that is easily deranged by the slightest untoward influence, the clinical progression is inveterately downward, with pronounced toxic secondaries (albuminuric retinitis, uremia, high blood-pressure), and almost complete lack of amenability to treatment. There is no primary disease of the glomeruli in primary contracted kidney, the atrophy developing as a result of vascular disturbance from primary sclerosis of the renal arterioles beginning relatively early in life from some unknown cause. What produces the primary disease of the smallest arterioles is still unknown, and we are equally in the dark as to whether the renal mischief precedes, accompanies, or follows a general disease of the vascular channels. The balance of information favors the idea that they are coincident. There is no doubt much justification for the claim made by pathologists that clinically too much emphasis is placed on the kidney element in so widespread an arterial disease as the primary vascular nephropathy. It is easier to criticise clinical procedure in this matter than to discriminate in practice. The clinician finds himself greatly embarrassed when it comes to appraising the relative value of heart, vascular, and renal changes in these widespread vascular renal degenerations. At least three types of cases are included in this grouping, *i. e.*, arteriosclerotic (senile) renal atrophy, genuine (primary ?) contracted kidney, and secondary contracted kidney. The first of these three has a comparatively unimportant renal aspect which ordinarily is better disregarded, but the kidney most certainly constitutes the important factor in the other two types. We have abundant proof, from nearly a century of pathological literature what difficulty the pathologist has experienced in solving this very problem, and no general agreement even now exists as to how arteries and kidneys stand as to pathological value in the development of contracting kidney. The difficulties of the pathologist are certainly no greater than those of the clinician in this connection. Since no definite symptomatic or urinary differences exist to distinguish one from the other form, discrimination becomes very largely a matter of judgment. Painstaking study of the clinical history and close observation of the progress of the case under treatment ordinarily suffice to separate predominantly renal from arterial cases, and the question of type must be left to the pathologist.

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[3] Arch. Int. Med., 1913, xii, 123.

Despite advances in our appreciation of the clinical problems of nephritis, the fact remains that in any given case it is impossible to predict accurately by clinical study alone what course the disease will take in development. To furnish grounds for more exact prognosis and more effective management, various methods have been devised for estimating kidney function in an effort to determine at any point in the progress of a case what amount of renal function remains and is available. If one wishes to gather all possible clinical data he will not rest content with a diagnosis of nephritis, but will proceed to determine the degree to which kidney function has suffered. This the functional test enables one in some measure at least to accomplish. Recent medical literature contains many contributions touching the subject of functional kidney tests, and it is now possible to approach the discussion of this question with considerable painstaking study available.[4]

[4] Rowntree and Geraghty, Jour. Pharmacol. and Exper. Therap., 1910, i, 579, ibid., 1911, ii, 393; Arch. Int. Med., 1912, ix; Vogel, Arch. Int. Med., 1911, vii; Baetjer, Arch. Int. Med., 1913, xi, 593; Foster, Arch. Int. Med., 1913, xii; Folin, Denis, and Seymour, Arch. Int. Med., 1914, xiii, 224; Agnew, Arch. Int. Med., 1914, xiii, 485; Frothingham and Smillie, Arch. Int. Med., 1914, xiv; Ibid., 1915, xv; Toleston and Comfort, Arch. Int. Med., 1914, xiv; Rowntree, Amer. Jour. Med. Sci., 1914, cxlvii, 352; Pepper and Austin, Amer. Jour. Med. Sci., 1913, cxlv, 254; Thayer and Snowden, Amer. Jour. Med. Sci., 1914, cxlviii; Fitz, Amer. Jour. Med. Sci., 1914, cxlviii; Arnold, Boston Med. and Surg. Jour., 1914, clxx; Stengel, Jour. Amer. Med. Assoc., 1914, lxiii, 1463; Austin and Miller, Jour. Amer. Med. Assoc., 1914, lxiii, 944.

All the tests employed for kidney function depend on the excretion of substances administered in known quantity which are recoverable more or less completely from the urine. Although not the first to utilize this method of investigation, credit belongs largely to Schlayer and his co-workers for bringing forcibly to the attention of the profession the possibilities of this means of research. Schlayer adopted the excretion of water and lactose as indicators of glomerular activity and of sodium chloride and potassium iodide as measures of tubular function. By using these substances as tests, according to a comparatively simple technique, Schlayer claims to be able to distinguish certain types of nephritis, there being a close agreement between the excretion of these substances and the respective types of renal involvement. According to Schlayer, vascular (glomerular) nephritis, whether acute or chronic, is characterized by delayed lactose excretion and by oliguria or polyuria according to the sensitiveness of the renal vessels and by a normal sodium chloride and potassium iodide excretion. Conversely, tubular nephritis is shown by a normal water and lactose excretion, and by delayed sodium chloride and potassium iodide excretion. All grades of mixed functional disturbances were found between these two extremes. In a general way it was claimed that the tests point out the severity of the disease, and as they are all delicate, these tests reveal disease at an early stage. Schlayer went so far as to submit a functional classification of nephritis based on the reaction to these tests. These conclusions are based on the assumption that we can test the individual functions of the kidney and presupposes a much more definite knowledge of the physiology of that organ than we in fact possess. Moreover, it is only in acute fatal cases of nephritis that anything like pure system involvement, glomerular or tubular, exists. So far as practical conclusions are to be drawn, too few observations are at hand to prove that functional findings revealed by tests furnish grounds for an anatomical diagnosis. Many considerations render the study of renal function in detail an extremely complex problem, and as the matter stands, the only available methods for clinical usage are such as furnish information regarding the total function of the kidney, their general excretory power. Tests for estimating the general excretory capacity have consisted mainly of the introduction of various dye substances which are excreted in the urine. General agreement accords first place among these tests to the phenolsulphonephthalein test of Rowntree and Geraghty, introduced in 1910; it was at first used most extensively in surgical cases, especially with reference to the question of operations on the urinary organs. It is equally applicable to medical cases, but the results are considerably more difficult of interpretation, and it is only recently that sufficient observations have accumulated to give it a fixed status in this class of cases. The harmlessness and simplicity of the test render it an easily available clinical procedure. In its application to nephritis, Rowntree and Geraghty have shown from careful studies that the amount of phthalein excreted varies in rough ratio to the extent of the renal damage. In fatal uremia only traces or perhaps none at all of the dye appear in the urine, while in mild and moderate grades of nephritis the amount recovered from the urine may be normal or nearly so. These authors claim, further, that in cardiorenal disease where the heart is failing and the kidneys are passively engorged a low phthalein output is observed at first, rapidly rising as the heart action improves and venous engorgement subsides. An increase in the phthalein index in such a case may be the earliest indication of restoration of compensation, and represents a favorable immediate prognosis. A low excretory capacity persisting after clinical evidence of cardiac improvement points to a severe nephritis and an unfavorable prognosis. Rowntree claims that the routine use of the test may occasionally bring latent kidney involvement to light, and cites the case of a boy who prior to the functional study was considered the subject of a diabetes insipidus, but who after one phthalein test was recognized as a case of advanced nephritis verging on uremia, a diagnosis substantiated at autopsy two weeks later. The authors of the test emphasize the purely empiric character of the investigation, owing to our lack of sound information as to the physiology of urinary excretion; and while attaching a high degree of prognostic value to the findings when positive, warn against a too general prognostic interpretation, inasmuch as the test yields information only so far as renal efficiency or inefficiency can be estimated, whereas death may occur in chronic nephritis from many other factors, cardiac and cerebral in particular, concerning which the test gives little if any information. This method, in common with other functional tests, must in consequence be considered in connection with general clinical study. The value of total function studies in acute nephritis is much less than in the chronic nephropathies because of the rapidity with which marked changes in functional output occur, ranging within a few days from a low reduction to normal. As a general rule, renal permeability is found markedly reduced in acute nephritis when the case appears clinically grave. This has been found to be the case also when acute exacerbations were associated with chronic nephritis at the time the test was made. In chronic nephritis previous to the employment of function testing, no amount of experience and training has enabled the physician to gain an accurate idea of the degree of the involvement of renal function. Perhaps the majority of cases of contracted kidney are clinically more or less latent, and serious or even fatal developments, among them uremia, may appear suddenly without their proximity being suspected. If function testing is applied as a routine, and repeated periodically, a much clearer view of the situation is secured. Not only may we be warned of the approach of uremia even when no indication of its proximity is revealed by clinical study, but the rate of progression of the nephritis may be followed.

Coincidently with the investigation of the functional adequacy of the kidneys in nephritis, attention has been directed to the estimation of the incoagulable or non-protein nitrogen of the blood as offering a valuable means for securing information of prognostic value. Strauss was the first to systematically study this phase of the nephritis problem. He found that there was generally an increase in the incoagulable nitrogen of the blood which he regarded as evidence of renal insufficiency. During the last few years there is notable in the literature an ever-increasing insistence on the significance of the non-protein nitrogen of the blood. Studies of this nature are particularly to be desired in the investigation of nephritis, for urine study cannot reveal the stage of accumulation of waste products, an accumulation that may vary from almost normal figures to enormous increase in uremia. The normal figures vary from 20 to 30 mgm. per 100 c.c. of blood, a ratio that may be many times increased in fatal uremia. Although the technic for non-protein nitrogen determination offers no difficulties to the well-equipped laboratory, it is unfortunately not readily available to the practitioner for routine clinical employment. Studies of renal elimination by the phthalein test consequently offer great advantage as to convenience and ease of application. The chief drawback attaching to this method of investigation lies in the interpretation of results, for it is quite conceivable that the rate of elimination of any one foreign substance may have no definite relationship to the efficiency of the kidneys in excreting metabolism products. Cases have been reported (Foster, Baetjer) in which the phthalein test gave practically normal figures, yet uremia resulted shortly after. As the non-protein nitrogen index in the blood is admittedly a more reliable criterion of renal efficiency, it is desirable to correlate the elimination of phthalein with the actual retention of nitrogenous waste in the blood. This has been undertaken by Frothingham, Fitz, Folin, and Denis in experimental uranium nephritis. The results of this investigation demonstrate that in general the tests parallel each other as indications of renal function, varying from normal during the course of the nephritis and returning to normal as the nephritis heals, with this essential difference: that whereas the amount of phthalein excreted shows the renal function at the time of the test, the amount of non-protein nitrogen of the blood measures the accumulating difference between the amounts of waste nitrogen products in the metabolism and the amounts excreted. The time element, the duration of the nephritis, is therefore an important factor in the result. It has been known for long that during the course of any nephritis there are certain periods when the urinary constituents are normal in amount as compared with the intake, and other intervals when they may be decreased or increased. These functional eccentricities of the kidneys, imperfectly understood, may have a bearing on some of the inconsistencies of the excretory tests. Frothingham and Smillie carried out a series of observations of the non-protein nitrogen and the phthalein test in 77 cases of chronic nephritis. From their charts it appears that the phthalein excretion steadily falls as the amount of non-protein nitrogen of the blood increases, the phthalein practically ceasing to appear in the urine when the non-protein nitrogen reaches 100 mgm. (three or four times normal). In a moderate number of cases a surprisingly low phthalein output was shown for which no cause could be found either from clinical findings or laboratory tests. They consider it fair to state that a considerable individual variation above or below the expected average may occur with the phthalein test for which no explanation can be found. They found the relation between the non-protein nitrogen and the clinical findings to be fairly exact. No non-nephritic cases showed accumulation. All the cases with non-protein nitrogen above 50 mgm. per 100 c.c. of blood gave clinical evidence of severe nephritis. In some of these cases the phthalein excretion was fairly good. On the whole, however, the non-protein nitrogen varied inversely with the excretion of phthalein in the urine. The accumulation of waste nitrogen seemed to be much less influenced by cardiac and other complicating factors than the phthalein excretion. Agnew undertook studies to determine what relation if any exists between phthalein output and non-protein nitrogen in the blood. He concludes that in general cumulative phenomena occur only when the phthalein excretion falls below 40 per cent. for two hours. This is in keeping with the conclusions of Folin, Denis, and Seymour. Tileston and Comfort found that cases of chronic nephritis without symptoms of uremia showed normal or only moderate cumulative signs, the uremic cases, on the contrary, showing a great increase in the non-protein nitrogen of the blood, the excretion of phthalein being roughly proportionate to the degree of retention. Rowntree, Fitz, and Geraghty show that chronic passive congestion of the kidneys gives rise to reduced excretion of phthalein in the urine without marked increase in the incoagulable nitrogen of the blood, and Agnew has been able by this contrast to separate cardiac cases from those having chiefly renal involvement. Austin and Miller report observations of the effect of sweat baths on the non-protein nitrogen of the blood in 11 cases of hypertensive renal disease. They find no evidence that sweating leads to any significant change in the blood waste accumulation. Thayer and Snowden attempt to throw some definite light on the clinical value of the phthalein test in prognosis by comparing the findings of the test with the anatomical alterations revealed at necropsy in 54 cases of nephritis of different types. In no instance of grave nephritis did they fail to find a material reduction in phthalein excretion. Their study reveals a progressive diminution in the output of the dye which they consider so definite as to give the test a considerable prognostic value. They conclude that there occurs in severe chronic nephritis a uniformly low phthalein excretion which, as a rule, in those instances not interrupted by an acute terminal process, decreases steadily up to the onset of uremia and is nearly or wholly suppressed from a day or two to a month before death. Acute terminal uremic developments which may be unsuspected clinically are common, and here a sudden diminution in the elimination of phthalein may come on in cases where the percentage previously excreted is not so low as to appear alarming. In not a single instance, and indeed not once in all their studies of five years, have these authors met with a good phthalein excretion in a case of severe chronic nephritis. Their observations with the test in 20 cases of chronic passive congestion from cardiac insufficiency conform with the findings of Rowntree and Fitz, and they consider it clear that chronic passive renal congestion alone may result in marked reduction of phthalein excretion which may return to normal as compensation is reëstablished. The foregoing discussion briefly reviewing the main facts brought out by investigation point to the high value of the estimation of the non-protein nitrogen of the blood in the diagnosis of uremia. That it constitutes the most reliable prognostic criterion we possess in chronic nephritis is beyond question. Owing to its greater clinical availability, great interest attaches to the reliability of the excretory test of Rowntree and Geraghty as a means of showing the proximity of uremia. Accumulating clinical observation and the fact that its results in the main parallel the estimation of non-protein nitrogen of the blood encourage the belief that its findings are within certain limitations reliable for prognostic purposes. A certain degree of latitude below expected normal figures should be allowed in carrying out this test, since it appears that only when the excretion of phthalein falls below 40 per cent. do cumulative phenomena develop. In interpreting its findings, it is to be remembered that the test shows the functional power of the kidneys at the time of the observation, and for the dye only, and its indications should not be trusted too implicitly or over too long a period without repetition of the observation. The influence of chronic passive congestion from cardiac causes is to be borne in mind. If excretory values are low and cardiac insufficiency is not present as a factor, we should not disregard the warning simply because clinical indications of uremia are absent, and, on the other hand, if symptoms indicate danger, their significance is not to be neglected merely because phthalein excretion is normal. No absolute prognosis as to duration of life appears possible on functional findings alone, because we do not yet know how low the phthalein excretion may go and yet be compatible with a renal efficiency sufficing to maintain life, provided the diet and hygiene of the patient are properly adjusted. It is extremely doubtful whether the phthalein test can be employed to any important extent in the diagnosis of nephritis. Routine observations with the method show an output well within the normal limits in the majority of cases classed as nephritis, with good cardiac compensation, except in severe cases, and when in long-standing involvement the actual physiological margin of active secreting tissue has been encroached upon. In so-called cardiorenal disease it is often a most puzzling problem to determine the relative importance of the renal moiety as compared with the cardiac and circulatory. It may happen that the evidence furnished by this method of estimating total renal function will help to elucidate this point. After some experience with the phthalein test covering a period of two years, I am encouraged to believe that it may be used to advantage in the clinical study of nephritis and high blood-pressure states generally. In most instances its value will prove a negative one, but at times and often when least expected a low excretory index will appear. Pending a repetition of the observation, such a case should be handled conservatively, and if the low ratio proves to be a fixed characteristic, and provided cardiac insufficiency be not present to discount the finding, sparing the kidney and brisk elimination must be the principles of treatment. In pending or actual uremia excretory values are minimal and possess the gravest significance. Every case of nephritis should have the test administered at intervals in order to keep track of the functional index, and perhaps thereby mark the progress of the disease. Moderate reductions are probably not of grave prognostic importance unless it can be determined by repeated tests that such is the established state of renal function.

The clinical and experimental research of recent years bears in many important ways on the problems of treatment. Except in rare cases we are still ignorant of the ultimate cause of chronic nephritis, and accordingly a causal therapy is still an ideal for the future to realize. The work of Rosenow, Billings, Eppinger, and others directs attention to chronic infections as an important etiological factor in obscure systemic disease. The fact that chronic septic foci may be latent for years in tonsils, teeth, sinuses, prostate, seminal vesicles, Fallopian tubes, etc., has but lately been fully realized. On the theory of intensity and duration of irritation, a principle well demonstrated in experimental nephritis, the possibility of chronic nephritis arising from low-grade prolonged sepsis must be reckoned with. In the case of an acute nephritis that fails to heal after the original causative infection has apparently disappeared, it becomes appropriate to inquire into the possibility of a persistent residual infective focus that is operating to render the nephritis chronic, and diligent search should be conducted to discover such a focus and to eradicate it. Since the toxic glomerular nephropathies are most often due to streptococcic toxins, the possibility of such a complication should be thought of in every case of streptococcic infection, especially tonsillitis. The urine should be watched carefully and convalescence attended to with more care than is usually done. As a matter of great clinical interest the recommendation of Billings[5] should be carried out. Every patient presenting evidences of nephritis or cardiovascular disease should be carefully examined with reference to previous infections which might be related to the existing disease and also for the presence of chronic focal infections somewhere in the body. When a focus of infection has been located and seems rationally related to the systemic condition, it should be eradicated if possible. We should not arrest investigation until search has been thorough and complete, for it is possible that two or more separate foci exist, and if we are to secure full prophylaxis all must be obliterated. This successfully attended to the chances of progression of supposed toxic secondaries may be greatly reduced.

The frequency with which chronic nephritis is found to exist in individuals who have been syphilitic for years makes it desirable to investigate this point in all cases where the etiology is obscure. The certain history of a primary lesion will, of course, at once direct suspicion in that direction, and an appeal to the Wassermann reaction may prove the point. Stoll[6] has recently directed attention to the importance of hereditary syphilis in the etiology of renal and arterial disease. The relationship of syphilis to arterial disease is well known, and it has long been familiar that syphilis may cause arterial hypertension. Schottmüller reports a positive Wassermann reaction in over 40 per cent. of his cardiac cases irrespective of the lesion. Congenital syphilis and even congenital syphilis in the parent may have the same effect on the fetus and infant as has acquired syphilis. Clinicians the world over have observed families in which many of the members succumbed to heart and arterial disease. It has been recently suggested that inherited syphilis might be an important factor in such instances, and the observations of Stoll apparently indicate that this is a fact. Cassel found renal changes in ten out of twelve syphilitic infants, and Murphy and Powers state that the renal lesion is, as a rule, a chronic nephritis sometimes latent and sometimes showing active periods. There is need of assigning to syphilis a far more significant influence in the etiology of arterial disease and the vascular nephropathies. Not only should the Wassermann test be carried out as a routine in obscure renal and cardiorenal disease, but a far more painstaking inquiry into the family and personal history should be made than is usually done. Death in middle life from cerebral hemorrhage of the patient's father, frequent miscarriages in the mother's personal history, or deafness in a brother or sister may possess the same etiological import as luetic stigmata or a positive Wassermann in the patient himself. The discovery of syphilis at once prompts resort to antisyphilitic medications. Hopes of improvement to the renal condition by this means are often doomed to disappointment. If the renal disease be not too far advanced a considerable influence over further progression may be gained, although advanced nephritis is more often harmed than helped. To push arsenic, mercury, or the iodides in advanced nephritis is to court disaster.

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[5] Arch. Int. Med., 1912, ix, 4.

[6] Jour. Amer. Med. Assoc., 1911, lxiii.

Before abandoning investigation into the etiology of obscure cases of chronic nephritis in the search for a causal therapy the prevalence and insidious nature of chronic lead intoxication should not be lost sight of. A careful inquiry as to the patient's occupation and environment should be made and the blood examined for basophilitic stippling of the red cells and the urine and feces tested out for lead. The history of exposure is the all-important factor in the diagnosis of plumbism. The significance of occupation and consequent exposure to lead absorption is shown by Hayhurst,[7] who found in varying degree the signs, symptoms, and after-effects of chronic plumbism in a total of 70 out of 100 painters apparently enjoying good health.

After all lines of investigation have proved unproductive, we are in most cases forced to fall back upon the mysterious world of metabolism and to accept such explanations as gout, hyperalimentation, persistent nervous overstrain, or other equally vague idea to account for the vascular renal degeneration. Errors in diet and faulty methods of living, although unsatisfactory as first causes, are nevertheless of quite considerable importance in perpetuating and aggravating existing renal lesions. Under careful management the condition of the average nephritis patient cannot only be greatly ameliorated, but the span of his life can undoubtedly be materially lengthened.

The history of diet therapy in nephritis is dominated by the principle of protein restriction. Modern research during the past twenty years has borne particularly on the mechanism and consequences of retention in nephritis, and the idea of sparing the kidney has been the first rule in diet. In acute nephritis, and during the acute inflammatory exacerbations of chronic nephritis, a large protein intake is undoubtedly unphysiological and exercises an unfavorable influence. During the stormy but relatively short session of acute nephritis the eliminative functions of the kidney are carried on with difficulty, the renal filter at times refusing even to pass water through it. Attention should consequently be concentrated on the diseased organ, and until convalescence is established, low food intake, even at times to the point of starvation, will best serve the interest of the patient. In such cases for the period necessary the nutritive problem may be submerged in the imperative needs of the choked and irritated kidneys. In chronic nephritis we are compelled to keep the general condition of the patient more in view. Granting the clinical justification of protein conservatism in the diet therapy of chronic nephritis, it is probable, speaking generally, that its severity and duration are much less influenced by manipulation of the protein ration than is commonly supposed. Our efforts in this direction have hitherto been governed by empiricism without scientific means of control, and we consequently have been far too much influenced by routine in the hope of controlling nitrogen excretion, which, after all, can hardly be considered an accurate measure of the gravity of a case. In chronic nephritis, nitrogen excretion is variable beyond explanation, and peculiar kinds of diet do not appear to influence it to any important extent. So far as can be seen at the present time the only reliable criterion available for regulating the protein intake in nephritis is the determination of the amount of waste nitrogen retention by blood analysis. That it is possible to reduce the urea and waste nitrogen of the blood to normal or less is abundantly proved by the feeding experiments of Folin, Denis, and Seymour,[8] and Frothingham and Smillie.[9] Cases with considerable retention require a restriction of protein, and by this means a return to normal figures may be brought about if the azotemia be not too severe. In cases of outspoken uremia no marked reduction of the azotemia results from a protein-free diet. Folin, Denis, and Seymour state that the response to the phthalein function test can be reduced by one-half before abnormal accumulation of non-protein nitrogen takes place in the blood. This estimate is in keeping with Agnew's statement that at 40 per cent. phthalein excretion cumulative phenomena appear in the blood. In clinical practice then it may be assumed that accumulation of waste in the blood begins at about the point where response to renal function testing by phthalein drops to 40 per cent. in two hours. Routine observations with this readily available test may thus enable one to appreciate, with much greater precision than is possible from clinical observation alone, the point (40 per cent. or lower) where positive protein restriction should begin. When the functional index is normal or nearly normal in contracting kidney it is difficult to understand what harm will result to the organs, provided no inflammatory element is present, from a protein allowance based on physiological

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[7] Amer. Jour. Med. Sci., 1914, cxlvii,

[8] Arch. Int. Med., loc. cit.

[9] Ibid.

needs. This being the case, we need no longer feel that some trifling miscalculation in the protein ration will jeopardize the welfare of the nephritis patient, nor that it is necessary to draw fine distinctions between various forms of protein. Aided by periodic functional testing to check up the condition of the kidneys, and with our present knowledge of physiological food requirements for good nutrition, the dietotherapy of chronic nephritis may be adapted with reasonable safety, if not, perhaps, with accuracy, and with due realization that in so chronic a disease, general nutrition and kidney conservation should stand on a parity.

Next in importance to the question of nitrogen balance and the protein ration in the diet of nephritis stands the interest that attaches to the ability of the kidneys to execrete chlorides. Since Widal called attention to chloride retention and its relation to edema, a salt-poor diet has been much employed, and while the results are not always as brilliant as Widal predicted, it has nevertheless become a well-established measure in the diet therapy of nephritis. In a general way the chloride excretion parallels nitrogen excretion in acute nephritis, although exceptionally it may fall below nitrogen or even below water. These are cases usually marked by dropsy. In chronic nephritis, chlorides do not run parallel to the urinary nitrogen. Although certain cases occur in which the chloride output is fully equal to the normal, more or less deviation is the rule. Subacute exacerbations of chronic nephritis determine definite periods of chloride retention, marked frequently by more or less edema, subsequent compensatory hypersecretion occurring as the dropsy subsides. In exceptional cases an inherent inability to excrete chloride may exist. A resumption of chloride function may frequently be brought about in such cases by withdrawal of salt from the diet. Observations on experimentally induced nephritis in animals seem to indicate that chloride retention depends on injury to the tubular structures of the kidney, whereas vascular (glomerular) changes produce no such effect. This fact may give us some insight into the underlying anatomical changes in certain cases marked by persistent chloride retention, although it is doubtful if such clear deduction should be drawn owing to the mixed type of nephritis encountered clinically. That chloride excretion is generally deficient in edema and that increase in chloride excretion coincides with disappearance of edema are clinical facts frequently observed. There is doubt, however, that the vogue of salt restriction, extensively and empirically enforced in all forms of nephritis, is justified by the established facts. Obvious contradiction to this practice is apparent in certain experiences with the so-called Fischer treatment of nephritis. The "fear of salt" apparent in the diet therapy of nephritis, subjects many patients to useless and burdensome hardship without care being taken to establish the fact that the kidneys actually retain chloride. Vogel[10] discusses this question and advocates a more rational and scientific procedure. Whatever may be thought of the salt-poor diet as a routine in nephritis, the indications to be secured from a study of the manner in which the kidneys deal with known amounts of sodium chloride and water are sufficiently valuable to render it advisable to make such determinations in beginning the treatment of at least severe cases of the disease. This is the more necessary, since in chronic nephritis with salt retention a long course of salt restriction is usually necessary to restore function. The technique of chloride tolerance determination is simple. For clinical purposes it is sufficient to conduct for a preliminary period of several days' observations on the amount of urine excreted, allowing the patient to follow his own inclinations as to the amount of fluid drunk, although this should be measured to compare intake with outgo. During this preliminary period the patient is on a mixed but tabulated diet, the chloride value of which should be approximately known. Each day a chloride determination of the twenty-four-hour urine should be made. As soon as it is found to be reasonably stabile, the water intake is doubled for two or three days, and the response in increased diuresis and the effect on body weight noted to determine water retention. Subsequently, the diet remaining stationary, 10 gm. of salt are added to the diet. This excess of salt should normally be excreted in from twenty-four to forty-eight hours, either by increase of salt concentration in the urine or by diuresis. The time of its excretion should be watched by determination in twenty-four-hour urines, and the effect on specific gravity, amount of urine, and body weight noted. This may be repeated at intervals of two or three days for control determinations. In this way the promptness and completeness of chloride excretion may be gauged and a proper basis secured for diet procedure. In cases appropriate for salt restriction it usually suffices to establish a "salt-poor" rather than a "salt-free" diet, an allowance of from 2 to 4 gm. per day being sufficient to produce the result desired without imposing any particular hardship on the patient. As stated above, a long course of salt restriction is needed to restore the excretory power of the kidneys, and the resumption of chloride feeding should be very gradual even after chloride equilibrium is established and edema has disappeared.

The practice of water restriction has been carried to excess in nephritis. Rarely can any advantage be gained by this procedure, except in certain cases of acute nephritis and in contracted kidney with cardiac dropsy. Nitrogen excretion is not influenced to any extent by the amount of ingested water, and in chronic nephritis with uremia fluid control has proved futile. In the early stage of certain severe cases of acute nephritis with oliguria the amount of fluid should be reduced to the smallest possible quantity. In such cases, to use an expression of Herringham, "the kidney is struck dumb," and for a period is unable to excrete even water; with recovery of function as the severity of the inflammation subsides, water may be progressively increased. The therapeutic problem in chronic nephritis is largely a cardiac one, the fate of the patient hanging almost solely on the maintenance of cardiac strength and an adequate blood-pressure; so that the justification for fluid restriction rests here upon the same basis as in primary heart lesions, *i. e.*, lessening of heart work. Regulation of fluid intake therefore becomes important as a prophylactic measure whenever the heart is to be spared, and also in all cases when edema makes its appearance whether the dropsy be cardiac or renal in origin. Regarding the influence on the height of the blood-pressure of free and restricted fluid intake, clinical observations indicate that it is practically without influence either way. So long as the heart is competent, unrestricted water drinking causes no material increase in blood-pressure, nor does limitation of fluids reduce blood-pressure values. Fluid restriction is called for in cases showing much dyspnea, arrhythmia, and other premonitions of cardiac breakdown. Even after heart failure has begun and edema is present we see good results follow this practice.

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[10] Arch. Int. Med., 1911, xii.

According to Strauss, the high blood-pressure of nephritis is usually, or at least frequently, accompanied by an excessive accumulation of nitrogenous waste products in the blood. This is in keeping with the prevalent clinical belief that the high pressures frequently observed in nephritis, and especially the "hypertensive crises," punctuating the course of many cases, are uremic in origin. One of the objects of the investigations undertaken by Folin, Denis, and Seymour already referred to was to determine whether there is any correspondence between the height of the blood-pressure and the accumulation of nitrogenous waste products in the blood. Their observations indicate that high blood-pressure is not necessarily accompanied by excessive retention of waste nitrogen, and they do not consider that high blood-pressure necessarily indicates the desirability of introducing low protein diet in nephritis. They state, moreover, that the wide fluctuations of blood-pressure, often amounting to 40 mm. or more, do not appear to be associated with any accumulative excess or marked variability in phthalein excretion. The observations of Frothingham and Smillie appear to bear out these conclusions, indicating that so far as uremia is concerned the height of the blood-pressure and the degree of pulse-pressure possess no clear prognostic value in nephritis. It is doubtful, however, whether these laboratory investigations are sufficiently numerous or conclusive to form a basis for the abandonment of the long-established clinical impression that the higher the blood-pressure the more imminent the danger from uremia. Of Janeway's series of 212 cases of high blood-pressure 46 died of uremia.[11] This group along with those dying of cerebral accidents showed the highest average for blood-pressure of any mode of death. Janeway's tables would indicate that, other things being equal, a systolic pressure of over 200 mm. constitutes at least a presumption in favor of termination by uremia or apoplexy.

Although it is true that many patients with a high blood-pressure in nephritis live for an astonishing length of time, the influence of this factor as a source of cardiac and arterial overstrain prejudices the course and finally determines the end of a large percentage of these cases. One of the aspects of chronic renal disease that has been considerably elucidated by experimentation is the pathogenesis of high blood-pressure. By performing successive reductions of kidney substance in dogs, Janeway has been able to demonstrate, after the lapse of several weeks following the completion of the operations, a material elevation of blood-pressure and polyuria, thus apparently establishing a relationship between blood-pressure and the amount of functioning kidney tissue. Thus the fact long recognized clinically that high blood-pressure, cardiac hypertrophy, and polyuria are rendered necessary in chronic nephritis to compensate for destruction of renal secreting tissue receives some support in experimental proof. The sound tissue that remains as the kidney shrinks, works on the borderline of maximal capacity, so long and only so long as its blood supply is maintained at a proper speed and a sufficient pressure. Under this mechanism the only way compensation appears possible is by further heart work at elevated pressure. This accounts for the relatively limited power of accommodation in the advanced stages of polyuric vascular nephritis and the absolute importance of the cardiovascular adjustment in maintaining renal function. From this view-point, if it be the proper one, it appears obvious that high blood-pressure and cardiac hypertrophy constitute a necessary evil that must be put up with, and if, as a consequence, death results from cerebral hemorrhage or heart failure, that is but an alternative to death from progressive uremia which would surely supervene without these cardiovascular secondaries. A good clinical illustration of their importance is furnished by the comparative well-being and symptom-freedom of patients during the stage of cardiac compensation contrasted with their miserable second state supervening with cardiac failure and secondary falling blood-pressure. In large measure, contracted kidney cases are for therapeutic purposes, cardiac cases, to be managed at one time as one would valvular disease during compensation and at another time as valvular disease with failing compensation. The degree of hypertension in patients under forty is most often in direct ratio to the element of uremia, and consequently we should view with concern a sustained high blood-pressure in the young and direct our treatment rather to the kidneys than to the heart. Here the phthalein test may give one important guidance. In older individuals many factors not present in youth enter into consideration, and this is the truer the farther we leave middle life; consequently we need not attach so much significance to high blood-pressure in the old. Cardiovascular degeneration in later life is not so directly proportional to the degree of pressure, other important factors such as arteriosclerosis entering into consideration.

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[11] Arch. Int. Med., 1913, xii.

It is possible for a patient with high and even very high blood-pressure to live for years without heart failure or apoplexy. Excessive blood-pressure values do not necessarily imply impending or early disaster. The state of the heart muscle and of the cerebral vessels is hard to gauge, and that is the deciding factor in prognosis and not the blood-pressure range *per se*.

The treatment of high blood-pressure is primarily hygienic. During the period of sustained compensation the entire personal hygiene, including diet, should be so regulated as to avoid all overstrain to heart and kidneys. The greatest emphasis is to be placed on this principle of treatment and no pains spared to enforce obedience in detail. Rarely is it advisable to lower the blood-pressure by direct therapeutic attack. This follows inevitably as a principle of conduct if we grant that high blood-pressure is a compensatory phenomenon. In chronic nephritis only discomfort, if indeed nothing worse, will accrue to the patient from the use of vasodilators. Nitrites should be reserved for emergency use to combat angina, stenocardia, cardiac asthma, severe high-tension headaches, and other pressure manifestations that may supervene in chronic nephritis. If dropsy, either renal or cardiac, exists, nitrites should not be given, as under these circumstances they do only harm. The appearance of dropsy in chronic vascular nephritis almost invariably signifies the advent of cardiac failure. Sooner or later in the course of every case that survives long enough, cardiac edema develops. Because the case is primarily a renal one it does not follow that the dropsy is of renal origin. It is usually cardiac, has the characteristics of cardiac edema, and can not be successfully treated by sweats and diuretics, but requires cardiac supporting measures. Digitalis in the end becomes the staff upon which the chronic nephritis invalid must lean. The reason for this is that after we have enforced the maximum of hygienic and dietetic control we can do no more for cardiorenal hypertension, but must wait until the heart begins to fail, and then we may prolong life for months or even years by the judicious use of digitalis and its congeners. The fact that the blood-pressure is high need not deter us from giving digitalis, since it acts just as well or even better with a high blood-pressure than it does with a falling pressure.

CHRONIC INTERSTITIAL NEPHRITIS AND ARTERIOSCLEROSIS.

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No agreement has as yet been reached as to the nature of and the progressive changes leading up to the granular kidney. Almost all the factors having to do with the carrying out of the normal kidney function, as well as the known factors giving rise to processes of fibrosis in other organs, have been mentioned as the inciting cause of renal sclerosis. Particular weight has been placed upon certain of these factors, because of their presence during one stage of the disease; but the opportunity of weighing their importance as an active cause for the contracted kidney has not been sufficiently good to direct a knowing finger at them. No one has yet been able to describe in a single instance the sequence of events from the beginning to the fully developed chronic interstitial nephritis. Thus, opportunity has remained open for wide speculation on the interpretation of the pathological processes involved.

Some attempt has been made to link up the clinical and urinary findings with the successive changes that are taking place in the tissues of the kidney. These, however, have added little to our understanding of the process. True it is, that with the fully developed disease, certain manifestations make their appearance, and we believe that some light has been thrown upon the correlation of the urinary character with the altered functional capacity due to renal sclerosis. But as for saying that the clinical manifestations bear any relation to the structural change of the kidney prior to the stage of granular contraction or, better, that we can forecast the outcome or even suggest the past processes in the kidney by clinical analyses we have no definite evidence.

Thus the problem has been left in the realms of conjecture and in the absence of incontestable proof by experiment, our knowledge concerning the development of the granular kidney has not materially advanced since the days of Gull and Sutton. In the face of this we do not wish to minimize the value of the many observations which have given us a clearer understanding of some of the finer reactions in the kidney substance; but it would appear that the minutiæ of some of these observations have led us astray from the broad aspects of the problem. That Jores should find a splitting of the internal elastic lamina of the renal arterioles, and from this finding discuss the importance of those still indefinite factors inducing arteriosclerosis as of prime importance for kidney disease, is, it seems to me, quite aside from the main issue.

For the main part, as was brought before the Association of American Physicians last year, studies upon the pathological nature of chronic interstitial nephritis have been made upon the advanced form of the disease. The criterion for the recognition of the important type of the disease is still based upon the description of the kidney as given by Richard Bright. If we adhere closely to these described characters, we will find there is a general similarity grouping them into one class. Gradually, however, our attention has been drawn to the fact that there are other forms of renal sclerosis, differing to a greater or less degree from the type here under discussion and readily recognized by careful observation and supplemented by the microscope. Thus we have kidney fibroses associated with hydronephrosis, ascending infection of ureter and bladder, hematogenous infection (pyogenic), infarcts, thromboses, amyloid disease, syphilis and other infective granulomata, and arteriosclerosis. But when we are speaking of the small, contracted or granular kidney we have in mind a diseased condition of the kidney which is different from each of these. It is different not only in the structural changes induced, but it is different also in its progress and in the distant systemic responses. The small, granular kidney is recognized by its small size, the thickening of its capsule with adherence to the underlying cortex. The kidney substance when stripped of its capsule is distinctly granular, each granule being surrounded by a depression from which fibrous tissue radiates parallel with the ascending vessels. The kidney substance may appear red, but, on the other hand, may be quite pale with not a few of its granules as yellow as the adrenal cortex. The cortex is most markedly altered, and is commonly only half the thickness of the normal structure. Within it are found many fine wedge-like sclerotic areas which occupy the positions between the granules observed on the surface. Alternating with these areas of fibrosis a fairly normal kidney tissue is observed. Along the patch of these radiating fibroses the tubules and Malpighian corpuscles become involved. The medulla is less altered, although a hyaline fibrosis not infrequently surrounds the excretory tubules. As in other regions subject to progressive fibrosis a considerable adipose tissue develops in the surrounding structures, particularly about the pelvis.

At the present time, opinion as to the development of this form of the interstitial nephritis has been divided mainly between two schools: the one considers it the outcome of a low grade but progressive inflammation, while the other believes it the result of a primary circulatory disturbance with a secondary atrophy and replacement fibrosis. Unfortunately the issue has been somewhat confused by the further introduction of the terms primary and secondary interstitial nephritis. Each group claims that their explanation is adequate for the so-called genuine contracted kidney. We would do well to drop such irrelevant terms and leave the application of a new nomenclature to him who clearly indicates the pathological sequence of events concerned in chronic interstitial nephritis.

Gull and Sutton considered the relationship of the arteries to the diseases of the kidneys as a peculiarly intimate one in which the arterial processes preceded and determined the interstitial nephritis. No agreement was reached by subsequent workers of the actual nature of the arterial disease, some viewing it as an endarteritis (Thoma), others as an hypertrophy (Johnson, Ewald, Friedmann), while the subsequent work by Prym and Jores drew attention to the arterial lesion as a true arteriosclerosis. Jores, furthermore, contended that the associated arterial changes in other organs, as was described by many, was also an arteriosclerotic process. The differentiation of this process rested upon the finding of deep arterial degenerations associated with a splitting of the internal elastic layer. As Jores, however, observed, arteriosclerosis may occur in the arteries of other organs in the absence of sclerosis of the renal vessels.

While the above authors were contending the dependence of chronic nephritis upon disease of the bloodvessels, Ziegler maintained the differentiation of types of chronic nephritis into groups associated or unassociated with arteriosclerosis. Those kidney lesions resulting from arteriosclerosis he believed to be individual and of a purely degenerative character, and designated them the arteriosclerotic kidney.

Both Jores and his pupils repeatedly remarked that chronic interstitial nephritis is a disease most frequently encountered in advanced life, a period when arteriosclerosis is also most prevalent. Nevertheless, they remark upon the finding of occasional cases in which they have been able to demonstrate advanced renal sclerosis unaccompanied by arteriosclerosis within the kidney. This agrees with the finding of Orth, who believes that in chronic interstitial nephritis the vascular changes are not essential because their variety does not correspond with the extent of the lesions. Roth described a number of cases in which renal sclerosis was advanced, but in which the arteries did not show the type of sclerosis defined by Jores as arteriosclerosis. He did, however, find that the arteries were affected by a connective-tissue thickening of the intima with splitting of the elastic lamina. As, however, processes of degeneration were wanting, he refused to call it arteriosclerosis. He suggests that these vessels might subsequently show arteriosclerotic change. From his observations we can only conclude that the kidney lesions have advanced with greater rapidity than those in the intima of the renal vessels, and his cases illustrate the point we wish to make that the narrowly defined form of arteriosclerosis as given Jores is not an essential factor in bringing out subsequent interstitial nephritis.

Roth described 3 cases of chronic interstitial nephritis without arteriosclerosis. In the kidneys, however, endarteritis was present in the small arteries. The cases were of relatively young individuals, and all of them had definite chronic or recurrent heart and arterial diseases. Yet with it all neither Jores nor his pupil sees any direct relationship insofar as a common causative factor is concerned in the simultaneous and progressive lesions in these three organs. These authors lay much stress on the finding of a single sclerosed arteriole or the mildest beginning of intimal degeneration as indicative of the influence of arteriosclerosis upon the kidney. No recognition is given to the fact expressed in their own cases that the fibrosis of the kidney was markedly advanced, and in the late stages of contraction, while the arteriosclerosis was only beginning. We can in no way follow the conclusion of this author as illustrated by his own cases that the chronic interstitial nephritis was the result of the early endarteritis demonstrated.

In the admirable work of Councilman (1897) the part played by the inflammatory process in bringing about the interstitial lesions of the cortex of the kidney was well demonstrated. In part, the cases studied included some of scarlet fever, diphtheria, pneumonia, and other infections, and the lesions described were of the nature of diffuse non-suppurative interstitial nephritis or types of glomerulonephritis. Of the latter, two forms were distinguished: a non-suppurative exudative form and a proliferative type. No clear distinction can be made between the etiological factors present in these two types, and it would seem that both may arise from the same causative factor. At the time of carrying out his work, bacteriological methods were not available to make a distinction between the various forms of streptococci, and we find the author speaking of the organisms isolated from cases of heart disease as pneumococci. I believe we will be correct in interpreting these results as indicating the presence of the Streptococcus viridans group. These organisms were found in cases of glomerulonephritis in large percentage, but the author's descriptions of the lesions indicate a transition between the glomerulonephritis and the diffuse, interstitial type. The work of Wagner bears out these findings, particularly in indicating the importance of the inflammatory process of scarlet fever and other infections in bringing about permanent interstitial change.

The work of Councilman is among the few in which a study of the progressive lesions of the kidney was accompanied by bacteriological examination. Of this he says: "Various forms of disease of other organs, particularly of the heart, are often associated with them, and bacteriological investigation has frequently shown in many cases the presence of certain organisms in the kidneys. In most cases the bacteria are found in some other lesion and in the blood, and their presence in the kidneys is but a part of a general septicemia. Moreover, the same conditions in the kidneys may be found associated with various organisms, and the same organisms may be associated with widely different anatomical lesions." A very fertile field awaits the routine study of the bacteriology of the kidneys in conjunction with the histological examination of all types of infection. The work which has been performed up to the present time is very suggestive of indicating the actual presence of bacteria rather than their toxins in the interstitial response of the kidney.

Undoubtedly what appears as complete disagreement in the personal observations on chronic nephritis lies mainly in the methods and material studied. Although the anatomical classification of kidney disease has not found favor with either the clinician or the pathologist, yet in the absence of a better substitute we all revert to this method. Müller attempted an etiological classification which as yet is hardly practical, and Herrick, while finding the old anatomical grouping unsatisfactory, offers nothing to replace it.

The types of nephritis which today attract our attention as the forerunners of the contracted kidney are the acute glomerulonephritis and the acute non-suppurative interstitial nephritis. Without desiring to describe the various types of glomerulonephritis, as well as the variety of interesting lesions that may be observed in the Malpighian body and Bowman's capsule, there is ample evidence that, in the human, these glomerulonephritides are infective lesions (Councilman, Gaskell, Baehr). The important feature lies in the fact that the glomeruli become the centres of inflammatory response in which a non-suppurative exudate and endothelial proliferation of the capillaries and a proliferative response of the inner lining of the capsule is commonly observed. The occlusion of the capillaries of the glomerulus by cellular proliferation or by thrombosis is only an added complication, and the subsequent degeneration that occurs in the tubules of the kidney is also to be viewed as a secondary disturbance depending upon vascular change rather than an injury produced by the primary factor.

A study of these cases of glomerulonephritis soon convinces one of the varying picture, even during the acute stage. In some thromboses of the glomeruli are common, in others rare, or the lymphocytic infiltration of the glomerulus is great and confined to this structure; others again, show the inflammatory reaction diffuse, surrounding Bowman's capsule, infiltrating the stroma between the tubules and following the course of the interlobular arteries and vessels of the intermediate zone. Many such cases have been described, by Councilman, Ziegler, and others. In fact, the picture presented by those kidneys in which the inflammation is more diffuse simulates more closely the type of acute interstitial non-suppurative nephritis. This latter type, which was originally discussed as a disease of the kidneys found after scarlet fever, measles, and sometimes smallpox, is now being incorporated with the glomerulonephritis, mainly because a certain amount of glomerular disturbance is always present. Fahr finds the streptococcus and pneumococcus most frequently associated with acute interstitial nephritis, and finds also that the same organisms are the chief cause of glomerulonephritis.

In short, although there are variations of glomerular lesions, and we encounter forms of inflammation of the kidney stroma, there does not appear to be any difference in the causative agent, most frequently the Streptococcus viridans. We must, however, point out that the bacterial infection reaches the kidney under different circumstances, and in a somewhat different form, in the various systemic diseases in which it is met. It is the bacterial clusters or small infective thrombotic masses which are liberated in heart disease that give rise to a type of glomerular infarction. In this way particular structures in the kidney are more intensely involved than others. So, too, in cases of bacteriemia, by organisms of low virulence, the kidney, as well as other organs, becomes a local focus of infection and this is particularly true in the bacteriemia of acute rheumatic fever in which the heart and bloodvessels are also affected. In these infections the heart may be involved in a variety of ways, and when the endocarditis becomes well-marked the kidney may be subject to embolic processes in its glomeruli, so that both the acute interstitial and the glomerulonephritis are simultaneously prominent. Hence it is obvious that to state that a definite type of kidney lesion is constantly to be found as a disease associated with infection of other organs is only voicing a rule with prominent exceptions.

The frequency with which acute interstitial and glomerulonephritis are present with infective heart disease is known to all who have observed these cases at autopsy and studied the tissues. It is, furthermore, easy to demonstrate the fate of the early inflammatory process. Fibroses of the glomeruli, of Bowman's capsules, and of the intertubular stroma may be demonstrated in all stages of formation, and recurrent attacks of these infective processes give rise to combinations of inflammatory responses in the kidney tissues. The question immediately arises whether the localization of these inflammatory processes gives us definite types whereby their future scars may be recognized. In answer to this the best reference is made to a few experimental results. In these it has been shown that inflammatory reactions in the kidney due to bacterial agents are prone to follow and surround the course of the bloodvessels particularly the interlobular vessels, and the ascending cortical branches as well as the afferent arteries of the glomeruli. Associated with these inflammatory responses there are not infrequently glomerular reactions, infiltrative, proliferative, or thrombotic. The progress of these lesions is similar to that in the human kidney and the end-result is a process of fibrosis radiating in its character with shrinking and granulation of the cortex and contraction of the entire kidney. Such lesions were reproduced in animals by the use of organisms (various members of the Streptococcus viridans group) isolated from infective heart disease, and the responses in the kidney were found to be accompanied by a myocarditis, at times an endocarditis, and in a few cases pericarditis. In only a few instances were systemic intimal arterial lesions obtained, although the perivascular response was always noted. Here, then, we have evidence of the development of the various stages of the contracted kidney in the presence of chronic infection and in the absence of primary arterial lesions.

These findings are in accord with the observations on human material and explain the occurrence of the contracted kidney in the first half of life as well as its greater frequency in the later years. Like all chronic diseases, the frequency of chronic interstitial nephritis is greatest in the late decades, and it is also a rather depressing outlook when we find that the incidence of these chronic diseases shall increase with the saving of more lives in childhood from death from scarlet fever, acute rheumatic fever, chorea, and other Streptococcus viridans infection. We must also equally appreciate that the heart and arteries suffer, sometimes much, at other times less, by invasion of these bacteria. In the arteries an endarteritis, a mesarteritis, and a periarteritis have all been repeatedly demonstrated in these infections during the early years of life. Of the heart lesions, we need make no other comment than reference to Aschoff's studies upon focal myocarditis, and of the frequent presence of endocarditis in the human and in experimental infections.

What, then, is the relation of renal arteriosclerosis to chronic interstitial nephritis? Before one can answer this we must have a clear understanding of the nature and genesis of arteriosclerosis. It is not enough to boldly speak of general arteriosclerosis as of common type and constant origin. Nor is this true within the kidney itself. There are arterial lesions within the kidney whose origin is widely different and which vary in their character.

Ziegler has long ago demonstrated the peculiar renal fibrosis resulting from peripheral arteriosclerosis. In old age, where it is not uncommon to have various arterial tracts severely involved in sclerosis and in which the lumina of the vessels are distinctly impeded, atrophic changes result in the area supplied. It is obvious that the amount of sclerosis varies greatly and is bound to pick out limited areas. The kidney tissues which suffer from the circulatory disturbances undergo atrophy, and even complete loss, without, however, necessarily showing evidence of intracellular degeneration (fat), as is otherwise so commonly encountered. The kidney shows areas of sharp depressions scattered irregularly over its surface so that its structure and shape are distorted. The individual depressions simulate those of infarct, but microscopically may at times be distinguished from these in that the involved areas contain some of the parenchymatous structures not completely destroyed. Furthermore, the kidney capsule is rarely adherent and the cortical surface between the areas of depression is relatively smooth.

Such depressions are the result of the obliteration of fairly large vessels within the kidney. At times, it may be, smaller vessels involving more restricted portions of the kidney are affected. This, then, leads to a local fibrosis of the glomeruli supplied by this circulation. Under these conditions the process, both in the glomeruli and tubules, is one of slow and progressive degeneration, with a secondary replacement fibrosis. It is unusual to observe under these conditions any evidence of an inflammatory reaction.

Compared with the granular contracted kidney, these changes in the arteriosclerotic kidney are quite different. It is inconceivable that a process of arteriosclerosis could so uniformly affect so many arterioles of a constant caliber to give the character found in the uniformly granular kidney. A comparable picture is to be observed in no part of the body, and we are well aware how uncertain is the distribution of arteriosclerosis. As the fibrosis following upon processes of degeneration in the atrophies of vascular scleroses is without inflammatory response, one misses entirely the presence of a granulation tissue and subsequent adhesions. The absence of these is noted in the freedom of the kidney capsule and in the lack of synechiæ about the glomerulus. Frequently, too, Bowman's capsule shows no thickening. Ziegler truly calls this the senile kidney.

It is, however, not common to meet with a clear-cut and uncomplicated case. The vascular scleroses of the kidney are most commonly the result of the same influence which has produced a primary inflammatory lesion in the kidney stroma. Hence, the development of scar tissue in the renal structures goes hand in hand with renal arteriosclerosis. Here, however, in the early stage, as well as during the years of progressive involvement, the kidney tissue and arteries show the presence of inflammation. These inflammatory deposits are easily recognized, and obviously vary in amount at the different stages. Jores has seen them in his interstitial nephritis, but has taken the view that no relation between the arterial disease and the inflammation can be determined. Like the results of the Streptococcus viridans infection upon the heart, giving rise to inflammatory processes differently disposed, so, too, this same infection, which is so frequently at the bottom of the fibrosis of the contracted kidney, brings about inflammatory reactions of varying intensity in different portions of its structure. The arteries appear to form the centre of distribution for these reactions, and much of the response is spent in the tissue surrounding the small vessels coursing through the cortex. To a certain extent, however, intimal reactions are also found. The latter, however, arise somewhat later in the course of the kidney disease, so that examples are not difficult to demonstrate in which intimal sclerosis is wanting while a non-suppurative inflammation is active about the vessel. Later, however, the picture is reversed and the intimal sclerosis attracts our eye. This is now the stage when appearances suggest that a close relation of cause and effect exists between the intimal arteriosclerosis and the renal fibrosis.

The intimal disease of the arteries most commonly met with in the late stages of chronic interstitial nephritis consists of a chronic endarteritis with deep, fatty change. The presence of a true hyperplasia of the musculo-elastic layer with secondary degeneration of the inner muscle bundle has never been met with by us, nor have its advocates ever clearly demonstrated its presence. The finding of splitting of the internal elastic lamina is now found to have no specific bearing on the problem of arteriosclerosis. McMeans (of our laboratory) has shown that such splitting is the common occurrence during inflammatory reactions of the intima.

Granted, therefore, that the early reactions which lead to the granular contracted kidney, simultaneously involve portions of the kidney parenchyma and its arteries, it is often extremely difficult to distinguish in the late stages of the disease exactly how much of the scar tissue has resulted through inflammation or as replacement fibrosis following arteriosclerotic atrophy. We should, however, continue to distinguish clearly the arteriosclerotic kidney of Ziegler from the granular interstitial nephritis, the former giving rise to true atrophic processes in the parenchyma with replacement fibrosis, the latter having an inflammatory basis for the development of connective tissue variously distributed about the important structures of the organ.

CERTAIN SYPHILITIC AFFECTIONS OF THE HEART AND AORTA.[1]

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A variety of morbid states of the heart and bloodvessels, all serious in nature, may develop during an attack of unquestioned syphilis. While the writer would not go so far as to say, with some recent investigators, that syphilis is the principal factor in the production of heart disease, it can at least be safely assumed that rheumatism and syphilis head the list as causes of organic injury to this organ. The advent of the Wassermann reaction has shown, in a convincing manner, that the role of syphilis as an etiological factor in diseases of the cardiovascular system had previously been underestimated. It is frequently the earliest clue to lues, especially in females, who, in many cases at least, know nothing of syphilitic infection, while in other instances a Wassermann reaction will, as has been well said, "unlock the tongue."

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[1] Read at a stated meeting of the College of Physicians of Philadelphia, June 2, 1915.

The cardiac lesions caused by the Spirocheta pallida are usually considered as belonging to the tertian stage of syphilis, but recent investigators have shown that they may develop soon after primary infection. Grassman[2] and later Brooks[3] and others have expressed the opinion that damage of a serious character may appear as early as the forepart of the second stage. The fact should not be lost sight of that both aortic and cardiac syphilis may be the result of hereditary lues. It is definitely known that the Spirocheta pallida has a selective action for the heart. As stated elsewhere, "of all the viscera the heart is among the earliest to become involved in this disease." The importance of recognizing the cardiac element at the earliest possible moment is further shown by the fact that involvement of this organ may develop soon after the primary infection without symptoms which attract attention until months or even years later.

The claim made by Landois, Citron,[4] Hausmann, Sears,[5] and others that lues may affect the heart alone is both interesting and important. In two infants who died, one at three months of inanition and the other at eight days of asphyxia, Warthin and Snyder found the Spirocheta pallida in the heart muscle, while neither histological lesions nor spirochetes were found elsewhere.

Among the commonest cardiovascular conditions due to syphilis are myocarditis, aortic regurgitation, angina pectoris, and mesaortitis, often resulting in aneurysm.

Mesaortitis. Since mesaortitis, with or without coronary changes, is commonly the primary complaint in cases in which, as frequently occurs, two or more of the affections named above are found in association, it will be considered first in this paper. That this condition is due in many cases at least to syphilis has been demonstrated both by postmortem evidence and the results of carefully conducted therapeutic observations. In 1910 Longscope[6] pointed out that a peculiar type of arteriosclerosis (mesaortitis) was frequently associated with aortic incompetency due to chronic aortic endocarditis. For example, in a series of thirty-seven autopsies showing mesaortitis a chronic aortic endocarditis occurred thirteen times, or in 35.1 per cent. Again, in 21 cases of chronic aortic endocarditis unassociated with lesions of any other valves occurring in connection with mesaortitis it was found that the lesions varied somewhat in extent in the individual instances, "but were always confined and often sharply localized to the arch of the aorta."

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[2] Deutsch. Arch. f. klin. Med., 1900, lxvii, 455; 1901, lxviii, 58 and 264.

[3] Amer. Jour. Med. Sci., October, 1913, p. 513.

[4] Berl. klin. Woch., 1908, xl, 2142.

[5] Archives of Diagnosis, January, 1913, p. 62.

[6] Jour. Amer. Med. Assoc., January 8, 1910, p. 118.

Of the 21 cases of aortic insufficiency associated with mesaortitis, 11 gave a definite history of either syphilitic infection or syphilitic lesion (gummata).

Harlow Brooks,[7] who made an anatomical study of the heart and aorta in fifty consecutive autopsies, found that 66 per cent., "including well and incompletely treated instances, died as a result of or with serious circulatory disease apparently of specific origin." Of these the myocardium was seriously involved in 44 cases, the coronaries in relatively greater degree than the general arterial system.

That this mesaortitis is of specific nature, with definite characteristics, is shown by the fact that the spirochetes have been found by Schmol and Wright in the lesions, the latter being able to demonstrate these organisms, often in enormous numbers, in all of five cases. Says Osler: "Microscopically the most important changes are found in the media and adventitia: (*a*) perivascular infiltration of the vasavasorum; (*b*) small-celled infiltration in areas of the media, with (*c*) splitting, separation, and destruction of elastic fibers and the muscle cells. The process is largely a productive mesaortitis, and so marked may be the foci in the adventitia and media that they look like miliary gummata, and, in fact, were so described as far back as 1877 by Laveran and by Heiberg."

ANEURYSM. The intimate connection between lues and aneurysm was well known to the older writers—to Pari, Larcisi, and Morgagni; but it has been specially emphasized by many modern writers, among whom the names of Osler, Heller, Koster, Chiari, Benda, and Klotz are conspicuous.

The belief that in persons under forty-five years of age syphilis plays the overshadowing role as an essential factor in causing aneurysm is confirmed by practically all of the more recent writers. On the other hand it may not be wholly gratuitous to caution the medical profession, as Hausmann has done, against regarding every case of aneurysm, even in syphilitic subjects, as due to lues.

Two additional facts may aid materially in distinguishing the etiological variety of aneurysm under discussion, namely, that the root of the aorta, *i. e.*, the ascending portion of the arch, is the usual seat of luetic aneurysms, and that they are frequently multiple.

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[7] Loc. cit.

Statistical evidence is not wanting to strengthen the view that syphilis is the most potent etiological factor in the production of aortic aneurysm. Cumston[8] quotes Rasch, of Copenhagen, who found twenty-eight aortic aneurysms in a series of 3165 autopsies. In 16 cases, or 57 per cent., syphilis was positively known to exist, while in 7 others, or 25 per cent., syphilis could be taken for granted in all probability. Etienne in a total of 240 cases of aneurysm found syphilis to be the cause in 166 cases, or 60 per cent. These figures have been amply confirmed by the following, among other percentages: Malmsten, 80; Heller, 85; Hampeln, 82; Pansini, 65.

My own collective investigations yielded a totality of 621 cases, of which number 363, or 58.5 per cent. were of luetic origin. In view of the fact that some of these cases had not been submitted to the Wassermann test, this percentage is too low. Among eight instances included in the above figures occurring in the Medico-Chirurgical Hospital, six were caused by lues.

A full discussion of the diagnosis of syphilitic thoracic aneurysm is not within the scope of this paper, but I desire to lay particular stress on a single fact bearing on this phase of the subject, namely, that a positive Wassermann reaction without confirmatory historical or clinical evidence (*e. g.*, age of the patient, site of the tumor-like protrusion, history of specific infection, etc.) does not warrant an assured diagnosis of lues.

Aortic Incompetency. Syphilis is now generally regarded as an essential factor in the causation of aortic incompetency, more particularly in cases which develop before the forty-fifth year of life. The chronic aortic endocarditis is commonly associated with mesaortitis, as before stated, affecting the root of the aorta, and, indeed, may be the result of direct involvement of the segments in such cases. It is worthy of note that this etilogical variety of aortic incompetency is often met with unassociated with widespread arteriosclerotic changes. In this connection it should be stated that a pure mitral lesion is seldom produced by lues, but a combined aortic and mitral lesion is commonly caused by syphilis.

There is a consensus of opinion to the effect that the most important etiological factor in the production of aortic incompetency is luetic infection. This view is amply supported by statistical observations. Thus Longcope[9] in a series of thirty-seven autopsies showing mesaortitis found thirteen instances of chronic aortic endocarditis (35.1 per cent.). Again, of 21 cases of aortic insufficiency, 11 either gave a definite history of syphilis or syphilitic lesions were discovered at autopsy. Citron obtained a positive Wassermann reaction in 10 out of 16 cases of this cardiac lesion, or in 62.6 per cent. Fiessenger[10] obtained a history of syphilis in 28 out of 37 cases of aortic insufficiency. Collins and Sachs[11] found a positive Wassermann reaction in 10 out of 13 instances of aortic valvular disease. Babcock[12] records 16 cases of aortic regurgitation, of which 11 were submitted to a Wassermann test with a positive reaction in all of the cases.

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[8] Archives of Diagnosis, January, 1913, vi, 25.

[9] Loc. cit.

[10] Bull. de l'Académie de Médecine, October 10, 1911.

My own collective investigations into the question of the frequent association of aortic insufficiency and syphilis embrace a total of 219 cases inclusive of the figures cited above. Of these 133, or 60.7 per cent., were clearly due to lues. In a considerable number of the cases of aortic incompetency no reference to the Wassermann test was noted. Obviously then the above figures underestimate the true role of syphilis in the production of this condition.

Severe pains may attend an invasion of the valve segments often accompanied by angina pectoris from implication of the coronaries in early cases developing more or less acutely. If the specific character of the cause be overlooked an inappropriate or the usual routine treatment of chronic valvulitis be adopted these cases may reach an early fatal termination. On the other hand, intensive antisyphilitic treatment may, if instituted early, bring about marked improvement, and the cases progress as aortic incompetency due to other causes.

While a certain diagnosis of syphilitic valvulitis affecting the aortic segments can not be made without a clear history of either specific infection or a positive Wassermann reaction, supported by confirmatory evidence, yet in the absence of rheumatism, gout, lead, alcoholism, pyogenic infection, or a predisposing occupation such cases should be labelled suspects and given the benefit of vigorous antisyphilitic treatment. Obviously, in instances belonging to this group the Wassermann test should be carried out, whenever possible, before remedial measures are instituted.

There are a few special physical signs which aid in the establishment of the luetic character of the chronic valvulitis. For example, Sachs[13] points out that "enlargement of the left ventricle is generally not so marked as in other forms of aortic insufficiency, and, therefore, the capillary pulse and double sound over the crurales are not so marked." I have observed the presence of a more decided arrhythmia in cases of aortic incompetency due to syphilis than in those due to other causes.

The early recognition of the true nature of the lesion becomes a matter of much practical importance, to the end that the ravages of this disease may be, to a great extent at least, obviated by suitable treatment. In this connection it should be pointed out that congenital cases of this affection may be due to hereditary lues.

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[11] Amer. Jour. Med. Sci., September, 1909, p. 344.

[12] Lancet-Clinic, August 15, 1912.

[13] Archives of Diagnosis, January, 1913, p. 62.

In cases in which the history is obscure too much stress can not be placed on the value of the Wassermann reaction as a means by which to determine the etiological variety in question. As in the case of aneurysm, so in aortic incompetency, a positive reaction alone unsupported by other clinical evidence does not warrant an assured diagnosis of lues, but it renders it highly probable that syphilis exists.

On the other hand it must be recollected that aortic incompetency occurring in a luetic subject may be due to causes other than syphilis, more especially if the valvular lesion develop after middle life. Here it should be noted that the cardiac lesions of syphilis usually appear within two or three years after infection, a fact of considerable diagnostic significance in some cases at least.

Myocarditis. As stated above, early involvement of the myocardium is not infrequent in the course of syphilis. Isaac Adler[14] first pointed out that the most important lesion of the heart is one of the myocardium, which lesion is dependent on periarteritis of the coronary vessels. Here it should be well understood that while endarteritis is the frequent important lesion, actual gummata in the myocardium are distinctly infrequent. Warthin[15] has described a syphilitic interstitial myocarditis in the absence of coronary periarteritis, and has demonstrated that the light-staining patches of proliferating stroma represent localized colonies of the spirochetes. Mareck, Simons, Buschke, and Fischer have also demonstrated the spirochetes in the diseased muscle of luetic myocarditis.

The recognition of incipient myocardial involvement is difficult, since the functional derangements thus produced are often slight, or, indeed, the condition may be entirely latent. The onset of the symptoms, if it develop in the secondary stage of syphilis, may be somewhat rapid or even acute. The principal features are arrhythmia, particularly intermittence and tachycardia, and less commonly extrasystoles. Brooks emphasizes among the earliest symptoms "irregularity of action, more marked when strain is added by mild exercises or through nervous apprehension;" he found the same thing true of the tachycardia, which is "incited to a degree by conditions which in the normal would fail to elicit such a response." Grassman writes: "I have studied 288 cases of secondary syphilis, and in 85 per cent. found disturbances of the rate and rhythm of the pulse, while in 40 per cent. accidental murmurs, usually with dilatation, occurred."

Pain is not a prominent feature, as a rule, in the early phases of the disease, although a feeling of thoracic oppression and slight dyspnea may be noted. In rare instances in which extensive lesions are present, actual pain with more or less tendency to radiation may be observed. The symptoms enumerated do not differ from those due to the myocarditis of other infections than syphilis, and it has been shown that these indications may all disappear in the course of a few days as the result of energetic antisyphilitic treatment—a fact that emphasizes the importance of an early recognition of the condition.

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[14] Trans. Assoc. Amer. Phys., May 3, 1898.

[15] Amer. Jour. Med. Sci., March, 1912.

In the tertian and quartenary stages of myocardial syphilis the symptoms and signs do not differ materially from those presented by myocarditis due to other causes. Not a few cases are latent and unsuspected during life, but are discovered if they come to autopsy. Soon or late in some cases dilatation is observed to occur, especially as the result of unwonted exercise, and this may be attended with a murmur.

Anginoid pains are not uncommonly present and obliterative endarteritis implicating the coronaries and producing myocarditis may result in attacks of true angina pectoris.

The markedly irregular character of the arrhythmia has been, as stated above, emphasized by Brooks, and his observation has been confirmed by my own experience. The observation first made by Runeberg, namely, tonelessness of the first sound at the apex, has since been confirmed by Callender[16] and others.

It is to be observed that neither a characteristic grouping of features nor a single pathognomonic symptom, unless it be a positive Wassermann reaction, are presented by the condition. As regards the Wassermann test it may be said that although a positive or negative reaction is not an absolute criterion of the presence or absence of a syphilitic infection, Brooks contends that it is better than the 70 per cent. of error based on the history or clinical findings alone.

Certain clinical peculiarities already mentioned may, however, serve to arouse suspicion of syphilis. Of these the tonelessness of the first heart sound and the decidedly irregular, accentuated character of the arrhythmia deserve special mention. Again, the association of phenomena which point to syphilitic involvement of other organs and structures of the body often throw light on the character of any cardiac lesion that may be present. Lastly, all determining causes of myocardial disease other than syphilis should be carefully excluded.

Heart-block is frequently caused by syphilitic lesions of the bundle of His, but this phase of cardiac lues can not be enlarged upon here. Suffice it to cite the figures of Robinson, who found that among 16 cases of heart-block due to such lesions 6 at least were of syphilitic origin.

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[16] Amer. Jour. Med. Sci., November, 1914, 706.

Angina Pectoris. The writer has collected 270 cases of angina pectoris from the literature, of which only 72, or 26.5 per cent. gave evidence of syphilis. This percentage, however, is much too low, since in 250 of the recorded instances no mention was made of a Wassermann test, sole dependence being placed in the history. The close association of syphilis and angina is amply confirmed by modern authorities. Breitmann,[17] of St. Petersburg, writes: "Every case of angina pectoris during the younger period of life is open to the suspicion of syphilitic origin." R. O. Moon[18] has been much impressed with the great predominence of lues in connection with true angina, and has seldom met with a case since the advent of the Wassermann test which did not give a positive reaction. Saundby[19] states that congenital syphilis as a cause of angina pectoris is not to be overlooked in young patients.

Prophylaxis. My discussion of the treatment of cardiovascular syphilis will be, owing to the exigencies of time and space, limited to prophylaxis. Doubtless the incidence of cardiovascular disease would be much lessened by a more systematic and vigorous treatment of luetic infection in general. There is perfect unanimity among syphilographers and clinicians of wide experience regarding the belief that when either syphilis of the myocardium of marked extent or aortic incompetency exists a cure is impossible of attainment.

Physicians should, therefore, feel themselves charged with a serious responsibility on behalf of the victims of luetic infection and carry out the treatment of early syphilis in the wisest manner possible. An added reason for adopting this course lies in the hazard arising from the administration of salvarsan or neosalvarsan in the severer forms of cardiovascular syphilis. It has been found that death, either occurring suddenly or after several days from the use of these agents, is commonly due to myocardial degeneration secondary to coronary lesions.

As stated elsewhere, "A sane view of the prophylaxis of cardiac involvement in this disease demands inclusion of the treatment of its secondary manifestations." It is in this stage that its development may take place, and also that the time of cardiac invasion can be fixed by the appearance of certain clinical features, in some cases at least.

In concluding the writer desires to make grateful acknowledgment of the assistance rendered by Drs. H. Leon Jameson and Andrew A. Anders in the work of searching the literature in connection with these statistical investigations.

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[17] Quoted by Bruce, Lancet, London, 1911, ii, 69.

[18] Clin. Jour., London, 1912-1913, xli, 353.

[19] Ibid., May 21, 1913.

A REPORT OF THREE HEART CASES SHOWING VAGUS INFLUENCE.

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and

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The three cases presented here occurred in the wards of the second (Cornell) division of Bellevue Hospital, and showed such points of common interest that they may well be grouped together.

Case I.—Sinus block, standstill of the heart. By these terms is meant a condition not only of skipped pulse and apex beats, but a dropping out of the whole cardiac cycle, either occasionally, frequently, or in sequence; periods of standstill[1] may be several seconds in duration.[2] It occurs as a result of vagus stimulation either by drugs (such as the digitalis series), by digital pressure, or by severe athletic exercise. Our purpose is to show that it is also produced by salicylic acid.

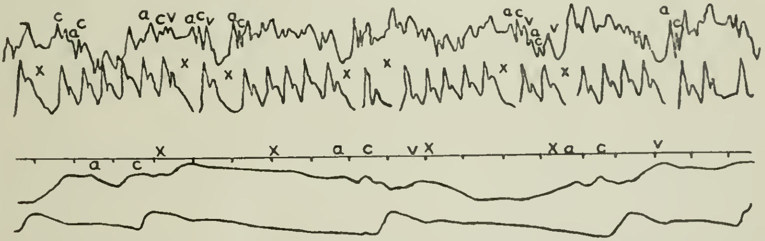

Fig. 1.—Sinus block induced by sodium salicylate. The tracings are from the same individual, and represent the same events; in the lower tracing the paper was moving faster, to draw out the curves for greater facility in reading.

Two years ago a woman came into the hospital in September, having taken salicylates during the entire summer; her pulse showed dropped beats which might well have been taken for ordinary intermissions or premature systoles; her apex also showed dropped beats which corresponded with the pulse intermissions; a tracing showed standstill of the whole heart during these periods. No other case came under observation until the present season, when a young man was admitted who was suffering from acute rheumatic fever, and who later developed endocarditis, pericarditis, and bronchopneumonia. His treatment consisted of salicylate of soda (20 grains every two hours for nine days), followed by tincture of digitalis (30 minims every four hours) for five days; a drop in pulse rate to 58 ensued, which disappeared when the digitalis was stopped. After a rest of four days, sodium salicylate (20-grain doses every two hours) was begun and continued for nine days, when block set in, to disappear after discontinuing the drug.

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[1] Mackenzie, Diseases of the Heart, 1908, p. 345.

[2] Laslett, E. E., Syncopal Attacks Associated with Prolonged Rest of the Whole Heart, Quart. Jour. Med., 1908–9, ii, 347.

The upper tracing shows normal *a–c* intervals, and shows also the lengths and frequency of the periods of standstill. The lower tracing shows one normal cycle followed by two successive periods of standstill, then two normal cycles; the *a–c* intervals are present and normal with each heart beat, and no event whatever occurs in the jugular tracing during the period of prolongation, showing that no impulse was generated at the sinus node. The resumption of rhythm in every instance here is normal; cases are reported in which slowing and irregularity are observed, the ventricles sometimes escaping first by premature systole.

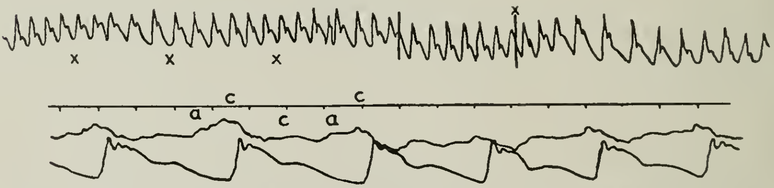

FIG. 2.—Effect of vagus pressure on a rapid heart; (the second tracing is normal and does not show the effect of pressure).

CASE II.—Increased heart action, normal in origin (sinus node), controlled by vagus pressure.

V. S., a man, aged fifty years, in previously good health, noticed upon exercise a little palpitation and an increase in pulse rate to 116; he was told by a consulting neurologist that he had heart block; physical examination showed nothing, however, but the increased rate on exertion and a sinus irregularity; there was no evidence of block. A sinus arrhythmia is evident; impulses are of normal origin and propagation was shown by the normal *a–c–v* intervals; the increased rate is noticeably slowed by right vagus pressure, but it immediately, though not suddenly resumes, its former rhythm upon removal of pressure; left vagus pressure shows no change in rhythm.

CASE III.—Paroxysmal tachycardia controlled by vagus pressure. Patient was a man, aged fifty-three years, who for two and a half months had had moderate edema, slight cyanosis, and dyspnea. Physical examination showed cardiac enlargement, with mitral leakage, increased blood-pressure, albumin and a few casts in the urine. He knew nothing about his paroxysms, and the first one came on after the exertion of sitting up in bed for examination.

The first tracing starts with normal rate and normal *a–c–v* intervals; the third beat is a premature systole; the fifth beat initiates the onset of the paroxysm, and the previous *a–c* sequence is now reversed to a *c–a* rhythm. The explanation is that with the onset of the paroxysm the auricular contraction falls back upon the preceding ventricular contraction and coincides with it, and this is true for every beat as long as the paroxysm lasts; in other words, the paroxysm is a series of premature auricular systoles. The paroxysm stops as suddenly as it begins, but the tracing has not caught the ending of it. The second tracing shows the paroxysm and normal period in fast time, but not in sequence.

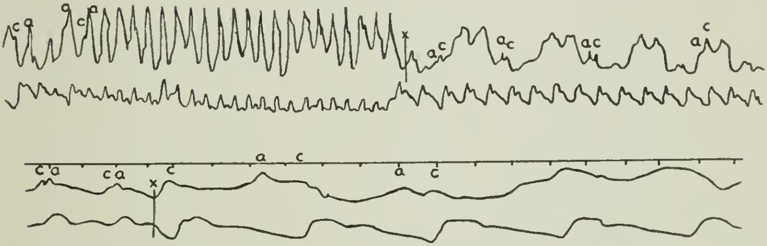

Fig. 3.—Paroxysmal tachycardia of auricular origin; the tracings show both the tachycardia and the normal period of action, in both the slow and fast time.

Pressure upon the right vagus produced no result after numerous trials; pressure on the left vagus caused the paroxysm to cease in three or four seconds, and never failed to produce this result; normal action lasted, however, but a minute or less, when the tachycardia gradually (not suddenly) returned; it again slowly disappeared, with pressure on the left vagus. The paroxysms lasted over a period of a few days, when they disappeared altogether.

Discussion. Pressure on the vagi has been frequently tried and often reported, but with variation in the results obtained. Lewis[3] has thought the pressure effects to be so irregular as to be unsatisfactory; he cites a case of 4-to-1 heart-block in which right vagus pressure stopped the ventricle altogether, and a case where left vagus pressure slowed the whole heart.

Cohn[4] helped matters greatly when he found (1912) that the right vagus is distributed mostly to the sinus node, sends a few fibers to the auricle, a few to the junctional tissue, and a few to the ventricle. The left vagus is distributed to the auriculoventricular node, sending a few fibers to the auricle, a few to the junctional tissue, and a few to the ventricle. Cohn[5] thinks the auricles are always affected by right vagus stimulation, and the ventricles may also be affected either primarily or secondarily; the ventricles are controlled by left vagus stimulation while the auricles may or may not be affected.[6]

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[3] Mechanism of the Heart Beat, p. 259.

[4] Effects of Stimulation of Vagi, Jour. Exper. Med., 1912, xvi, 732.

Robinson and Draper[7] studied the pressure effects on four children with endocarditis. Right-sided pressure slowed the rate of the heart-beat sometimes to such an extent that the ventricles assumed a rhythm of their own. Left vagus pressure controlled the rate of stimulus conduction. These results were the same as those obtained upon dogs, for Robinson[8] found that cutting the left vagus and stimulating the right stopped the whole heart; cutting the right and stimulating the left slowed but did not stop the auricles, but did produce increased difficulty in transmitting impulses from auricle to ventricle, so that heart-block resulted in varying degrees.

CONCLUSIONS. Case II of the series presented in this paper, a case of simple increased frequency of the heart's action, was controlled and slowed by compression of the right vagus governing the sinus node, the slowed impulses from which were transmitted through junctional tissue to the ventricles, maintaining normal rhythm; this is what one would expect.

Case III, tachycardia of auricular origin, was slowed by compression of the left vagus. Why was not this influenced by right vagus pressure as was the former one, both being of auricular origin? The answer must be found in Robinson's statement[9] that each nerve has to a lesser degree the function which predominates the other. Whether the ventricles were affected first, the auricles falling in line, or whether the subordinate fibers running to the auricles were first stimulated, the ventricles following by sequence, we have no way of knowing; the latter reasoning is the most likely one, as the paroxysm was not of ventricular origin, this being rare under any conditions.

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[5] Auricular Tachycardia, with a Consideration of Differences Between the Vagi, Jour. Exper. Med., 1912, xv, 49.

[6] Cohn and Fraser, Paroxysmal Tachycardia and the Effect of Stimulation of Vagi Nerves by Pressure, Heart, v, No. 1.

[7] Action of Vagus Nerve on Human Hearts, Jour. Exper. Med., 1911, xiv, 217; 1912, xv, 14.

[8] Influence of Vagus Nerve on the Dog's Heart, Jour. Exper. Med., 1913, xvii, 429.

[9] Loc. cit.

THE "SUGAR" CONTENT OF THE SPINAL FLUID IN MENINGITIS AND OTHER DISEASES.

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The growing interest in and investigations of the origin and function of the spinal fluid have led to the study of this phase of the question, namely, the carbohydrate content or reducing substance of this fluid. The question is not only of theoretical interest in regard to the origin of the fluid and its relation to the blood serum, but also it is of definite practical value from the standpoint of early diagnosis and prognosis in meningitis and possibly in syphilis.

Repeated and exhaustive studies have been made of the physical, chemical, and biochemical properties of the spinal fluid in health and disease, and while attention has been given to the quantitative analyses of albumin, globulin, urea, etc., but little notice has been taken of the actual amount of the reducing substance. Tests, including Fehling's, Williamson's, Trömmer's, phenylhydrazin, fermentation, etc., have been utilized, the results in the hands of different workers being by no means of one accord; however, the conclusions of those who have made the most careful and prolonged studies indicate that this substance is chiefly glucose, though mucinoid matter, pyrocatechin, etc., may be present (Mestrezat,[1] Quincke,[2] Nawratzki,[3] Connal,[4] von Jaksch,[5] Trerotoli[6]). A few authors have made quantitative analyses over a limited number of cases, the results of which are variable and the estimations too few to be of real value.

Von Jaksch in 20 normal cases found 0.06 to 0.08 per cent.; Nawratzki, using Allihn's method, found 0.046 per cent.; Kopetzky,[7] with Benedict's method in 8 cases, found an average of 0.046 per cent. Mestrezat gives a table of all the constituents of both the spinal fluid and blood serum in 20 cases, the average concentration of the reducing substance of the fluid being 0.048

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[1] Jour. de Phys. et de Path. gén., 1912, No. xiv, pp. 504-508.

[2] Quoted by Neuberg (note 8.)

[3] Zur Kenntnis der Zerebrospinalflüssigkeit, Ztschr. physiol. Chem., 1897, Bd. xxiii.

[4] The Cerebrospinal Fluid, Quart. Jour. Med., 1909-10, No. 3, p. 152.

[5] Klinische Diagnostik innerer Krankheiten, 5th Aufl., 567.

[6] The Spinal Fluid in Nephritis, Ann. d. facolta di Med., 1913, Bd. iii, Nr. 3, S. 101-324.

[7] Zeitschr. f. Ohrenheilk. u. f. d. Krank. d. Luftweg, 1913, Bd. lxviii, H. 1, S. 1-19.

to 0.053 per cent., and from these findings he supports the dialysis theory of the origin of spinal fluid, believing that beside the secretion there is a dialysis of blood plasma by means of epithelial differentiation, the constituents of both fluid and blood being so similar. My results in a series of normal cases reveal values of from 0.06 to 0.075 per cent., thus confirming the findings of von Jaksch and to a certain extent of Neuberg,[8] but being considerably higher than the values in the few cases given by the other workers.

The Relation of Blood Sugar to Spinal Fluid Sugar. In regard to the relation between blood sugar and the sugar content of the spinal fluid, Neuberg states that the content is the same in both. Using the same method (Bang's) for the estimation of the sugar content of both, I have found that in health the concentration in the blood averages about 10 mgm. per 100 c.c. higher than that of the fluid. This is of interest when we recall the studies of Goldmann,[9] who, by means of intravital staining, in his experiments upon the fetal nervous system of animals, discovered that intracellular glycogen was demonstrable only in the plexus cells. This substance, unlike the dye, was not held back by the cells but secreted drop by drop and diffused with the cerebrospinal fluid throughout the entire nervous system. Yoshimura[10] also demonstrated glycogen in the vacuoles of the epithelial cells of the choroid plexus. These discoveries when considered with those of Mott,[11] Pettit and Girard,[12] Dixon and Halliburton,[13] Frazier and Peet,[14] etc., present very forcible arguments in favor of the secretory origin of the fluid. They likewise bear convincing evidence of the presence of glucose in the spinal fluid, for until recently many have maintained that other substances than glucose were responsible for the reduction of copper.

In meningitis investigators have shown, as have I in a recent article,[15] that the blood sugar is considerably increased. On the other hand the sugar content of the fluid is materially decreased. It may be possible that the hyperglycemia in this disease is accompanied by an initial increase in the sugar content of the spinal fluid and that this latter increase is more than offset by the destructive activity of the organisms present, a condition which will be referred to later. The hyperglycemia in the majority of other disease in which I have had an opportunity of studying simultaneously the blood and spinal fluid has usually been accompanied by a corresponding rise in the sugar content of the fluid, the figures being almost constantly somewhat lower in the fluid than in the blood.

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[8] Der Harn sowie die übrigen Ausscheidungen und Körper Flüssigkeiten, ii Teil, Berlin, 1911, S. 1019.

[9] Experimentelle Untersuchungen über die Function der Plex. Choroid. und der Hirnhaüte, Arch. f. klin. Chir., 1913, ci, No. 3, S. 735.

[10] Arbeiten aus dem Neurolog. Instit. d. Wiener Univ. (Obersteiner-Hefte), Bd. xviii.

[11] Quoted by Frazier and Peet (note 14).

[12] Ibid.

[13] Journal of Physiology, 1913, vol. xlvii, No. 3, pp. 215–224.

[14] Amer. Jour. Physiol., 1915, vol. xxxvi, No. 4.

[15] Hopkins, A. H., Studies in the Concentration of Blood Sugar in Health and Disease, Amer. Jour. Med. Sci., February, 1915, No. 2, vol. cxlix, p. 254.

Table I illustrates the variations that may occur in this relationship in disease.

TABLE I.—TABLE ILLUSTRATING THE VARIATIONS IN THE RELATION OF THE SUGAR CONTENT OF THE SPINAL FLUID TO THAT OF THE BLOOD IN DISEASE

Case.	Name.	Diagnosis.	Reducing substances in spinal fluid.	Blood sugar.
1	Ell.	Hemiplegia; apoplexy	0.078	0.169
2	Carr.	Subarachnoid hemorrhage	0.075	0.182
3	Hub.	Brain tumor	0.081	0.085
4	T.	Pituitary tumor (?)	0.074	0.077
5	Don.	Brain tumor (?)	0.070	0.080
6	Ke.	Syphilis	0.034	0.070
7	F. J.	Syphilis	0.053	0.085
8	Sp.	Syphilis; tabes	0.047	0.088
9	B. R.	Tuberculous meningitis	0.029	0.092
10	Dd. T.	Tuberculous meningitis	0.027	0.139
11	D.	Diplococcic meningitis	0.015	0.080
12	Ca.	Idiot; castration	0.085	0.105
13	D. S.	Idiot; castration	0.087	0.102

TECHNIC. The method employed is a slight modification of Bang's[16] recent micromethod for the determination of blood sugar, this having proved to be very useful as a rapid and reliable clinical test.

As only three or four drops of fluid are needed it affords possibilities for the study of practically every fluid withdrawn, and at the same time gives accurate results as the protein content of the fluid is thoroughly separated before the reduction of copper takes place.

The disadvantage of Fehling's test as at present used in many laboratories is that in fluids in which the protein content is high the reduction of copper is masked by the biuret reaction, and entirely erroneous results are thus not infrequently derived in the very cases in which the quantity of reducing substance is of most importance, as in meningitis. Further, the results are also unreliable if no definite amounts of the alkaline and copper solution are used and if the amount of dilution is not carefully regulated. Varying amounts of dilution give varying results, so that I have tried to establish a uniform method by controlling Fehling's with accurate quantitative estimations. In the majority of cases the Fehling test was applied at the time of Bang's test, and after using different dilutions I found that 1 c.c. each of the copper and of the alkaline solutions diluted with water to 15 c.c. and the addition of exactly equal parts of this solution and the fluid gave fairly constant relative results in all cases in which there was not a great increase in protein content. In the latter cases the results were not so clear cut, owing to the deep purple biuret reaction. The fermentation test was used in a few cases with positive results while the controls by Benedict's[17] new colorimetric method, for which I am indebted to Dr. G. K. Strode, are given in Table II. Estimations were made over a series of 141 cases of various diseases, in a number of which the blood sugar concentration was studied at the same time.

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[16] Der Blutzucker, Wiesbaden, 1913; Bioch. Ztschr., November, 1913, H.$\frac{3}{4}$, B. 57. Two or three drops of the fluid are taken up on the small specially prepared and weighed filter papers, the rest of the technique being carried out as described by Bang in his monograph, "Der Blutzucker." The only modification which I have used has been the subtraction of 0.07 c.c. from the amount of iodine required in the titration for the quantity of reduced copper. Bang in his test for blood sugar subtracts 0.12 c.c. from the iodin titration, claiming that the copper and alkaline solution neutralize 0.06 and that other substances than glucose in the red blood cells require another 0.06. In testing my copper and alkaline solutions, I found that 0.07 c.c. iodin was required, and hence that amount was subtracted.

TABLE II.—ILLUSTRATING THE CONTROL OF BANG'S METHOD WITH BENEDICT'S COLORIMETRIC METHOD.

Case.	Bang.	Benedict.
1	0.087	0.086
2	0.066	0.065
3	0.071	0.099
4	0.068	0.061
5	0.066	0.052
6	0.116	0.134
7	0.084	0.077
8	0.062	0.044
9	0.053	0.058
10	0.027	0.000
11	0.107	0.115
12	0.104	0.116

MENINGITIS. The early diagnostic and prognostic value of the test for glucose in the spinal fluid has been emphasized by many. Sicard and Roussea,[18] Silvestrini and Nestri,[19] Mestrezat, Kopetzky, Connal, Jacob,[20] etc., found it markedly reduced in meningitis. Kopetzky remarks upon the necessity of sugar as a medium for the growth of many bacteria and that the prompt examination of the spinal fluid in suspected cases of meningitis is specially urgent, as it is generally known that with bacterial invasion of the meninges there is a rapid reduction in the glucose of the fluid, and hence the earliest and most important clue may be given by the discovery of a reduction of glucose, a view supported by Connal, Kaplan, and others. Accepting these findings and confirming them by my results in quantitative analyses of twenty cases it is evident that the test is of practical value in distinguishing between meningitis and the so-called "meningismus" accompanying pneumonia, typhoid fever, etc.

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[17] Jour. Phys. Chem., October, 1914.

[18] Quoted by Trerotoli, A., Note 6.

[19] Ibid.

[20] British Med. Jour., 1912, p. 1096.

From the prognostic standpoint it has been found that as the bacteria loose their virulence and their ability to break up sugar and as they become more difficult to cultivate from the fluid, the sugar content gradually increases and is in turn followed by convalescence. This increase may be ascertained by repeated lumbar punctures even before clinical improvement has been observed, and hence its value as the earliest sign of improvement. Investigators have evidently overlooked the fact that the injection of Flexner's serum in the treatment of this disease is probably responsible for the immediate rise in the reducing substance. I find that this serum is higher in its sugar content than normal blood serum, the average being 0.11 per cent., a figure considerably higher than that of the normal spinal fluid. Table III illustrates the results in a series of cases of meningitis. As these fluids were contributed from the laboratories of various hospitals it has not been possible to make simultaneous studies upon the blood sugar in many instances.

TABLE III.—MENINGITIS.

Case.	Name.	Diagnosis.	Reducing substance.
1	Bl.	Tuberculous meningitis	0.035
2	Bl.	" "	0.048
3	E. G. Mc.	" "	0.037*
	E. G. Mc.	" "	0.038
4	B. R.	" "	0.046
5	F. E.	" "	0.017
6	C. W.	" "	0.020
7	F. C.	" "	0.023
8	D. D. T.	" "	0.032*
	D. D. T.	" "	0.027
9	B. R.	" "	0.035*
	B. R.	" "	0.019
10	D. F.	" "	0.046
11	D. G.	" "	0.033
12	J. W.	" "	0.033
13	A. Y.	" "	0.037
14	A. E.	" "	0.066*
	A. E.	" "	0.053
15	Mc.	" "	0.027*
	Mc.	" "	0.030
16	Dr. T.	" "	0.020
17	Da.	Diplococcic meningitis	0.015
18	J. C.	Pnemococcic meningitis	0.016
19	A. D. P.	Acute meningitis	0.008
20	Mac	Acute meningitis	0.048
21	J. R.	Acute meningitis	0.018
22	R. S.	Diplococcic meningitis	0.031
	R. S.	Diplococcic meningitis	0.079†

* Values obtained on different dates.

† Twenty-four hours after the administration of Flexner's serum.

The results show consistently low figures, which in a few instances were repeated at different dates. It should be noted that Fehling's reaction, though slight, was not altogether absent, although frequently considerably masked by a strong biuret reaction, owing to the increased protein content.

Diabetes. This series of diabetes (Table IV) gave interesting results, as there was a striking increase in the sugar content of the fluid which, however, usually remained lower than that of the blood.

TABLE IV.—DIABETES.

Case.	Name.	Reducing substance in spinal fluid.	Blood sugar.
1	U.	0.163	0.187
2	G.	0.149	0.221
3	K.	0.131	0.169
4	B.*	0.623	0.660
5	P.	0.174	0.223
6	M.	0.187	0.174
7	McM.	0.112	0.134
8	T.†	0.074	0.077

* In coma five hours before death.
† Glycosuria persistent.

The reduction of Fehling's solution was, as a rule, complete when the dilution was 1:15, but in other dilutions the reactions were variable, though always marked. In the few cases mentioned by other investigators an increase in the sugar content has been noted, Fehling's qualitative test being the one employed.

Infections. In this short series (Table V) the values lie approximately within normal limits and require no comment other than a reference to the recent paper of Rohdenburg and Vander Veer[21] on the question of spinal fluid in pneumonia. Being impressed with the mental depression so often encountered in this disease, they made a chemical and bacteriological study of the spinal fluid in a series of cases irrespective of the occurrence of meningeal symptoms and in which only one case showed pure meningitis. Of the fatal cases, 87 per cent. showed pneumococci in culture, while in those of favorable termination 34 per cent. gave positive cultures. They further state that all fluids giving positive cultures were positive

TABLE V.—INFECTIONS.

Case.	Name.	Diagnosis.	Reducing substance.
1	G. H.	Measles	0.063
2	D. M.	Pneumonia	0.061
3	Ger.	Pneumonia	0.063
4	J. C.	Pneumonia; dementia precox	0.063
5	C. W.	Bronchopneumonia; nephritis	0.085
6	Vet.	Poliomyelitis	0.077
7	R. B.	Septicemia; nephritis	0.036
8	M. M.	Septicemia; pyelitis	0.116
9	C. S.	Pulmonary tuberculosis	0.057
10	T. M.	Articular rheumatism	0.080
11	Rei.	Tetanus	0.077

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[21] The Spinal Fluid in Pneumonia, Jour. Amer. Med. Assoc., 1915, No. 15, vol. lxiv.

for both sugar and globulin, but as no reference is made as to the method employed for the sugar determinations the relative variations are lost. These authors conclude that pneumococci are very frequently present in the spinal fluid in pneumonia and that the early lysis of these organisms, with the liberation of the endotoxin in close proximity to the vital centres, offers a ready explanation of the profound and sudden cardiovascular collapse as well as the mental symptoms of the disease so often noted, for in patients in which positive cultures were obtained from the fluid, profound depression and frequently delirium were noted.

INTOXICATIONS. In this series (Table VI) morphin did not influence the sugar content; alcoholism gave inconstant results. Case 6, being one of delirium tremens, showed a pronounced increase. Case 7, acetanilid poisoning, was studied a few hours before death. The low value obtained in Case 8, atropin poisoning, is interesting in view of the secretory theory and of the possible action of atropin upon the choroid plexus, though Dixon and Halliburton state that atropin does not check the secretion in dogs when administered in the usual size doses.

TABLE VI.—INTOXICATIONS.

Case.	Name.	Diagnosis.	Reducing substance
1	McD.	Morphinism	0.073
2	J.S.	Morphinism and heronism	0.075
3	B.D.	Alcoholism	0.096
4	G.B.	Alcoholism	0.056
5	J.C.	Alcoholism	0.071
6	E.B.	Alcoholism and delirium tremens	0.129
7	A.E.	Acetanilid poisoning	0.139
8	J.S.	Atropin poisoning	0.057
9	H.B.	Alcoholism; arteriosclerosis	0.073
10	A.T.	Alcoholism; cirrhosis of liver	0.050

NEPHRITIS. Trerotoli, in his exhaustive monograph on the *Spinal Fluid in Nephritis*, considers that the influence of renal impermeability is mirrored by the chemical composition of the spinal fluid. He notes the importance of the increased urea content specially as a sign of impending uremia, a fact recently recalled by Soper and Granat,[22] who also emphasize the value of quantitative estimations for both diagnostic and prognostic use. Mestrezat, in a few cases of uremia, reports an increase in the sugar content of the fluid.

In this series of 14 cases, several of which were complicated by other conditions, 7 cases gave high values, 6 of the latter being uremic and in these the blood sugar, when estimated, also revealed an increased concentration. Here it must be recalled that a moderate hyperglycemia occurs in some hypertension nephritics. From the low value in Case 13 I suspect meningeal involvement, as the case was complicated by a septicemia. Although Case 5, uremia, had been receiving a 5 per cent. glucose solution by rectum for fourteen hours the content of glucose in the fluid was not unusually high (Table VII).

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[22] The Urea Content of the Spinal Fluid, with Special Reference to its Diagnostic and Prognostic Significance, Arch. Int. Med., 1915.

TABLE VII.—NEPHRITIS AND UREMIA.

Case.	Name.	Diagnosis.	Reducing substance in spinal fluid.	Blood sugar.
1	C. B.	Uremia	0.104	—
2	R.	Uremia	0.127	0.149
3	M. L.	Uremia	0.072	0.127
4	Ba.	Uremia	0.093	0.144
5	K.	Uremia	0.089	—
6	A. A.	Uremia; acute parenchymatous nephritis	0.084	
7	G. W.	Uremia	0.092	
8	J. McV.	Acute parenchymatous nephritis	0.072	0.087
9	Ne.	Chronic interstitial nephritis; syphilis	0.068	0.073
10	C. W.	Nephritis; pneumonia; parotitis	0.139	—
11	N. S.	Chronic nephritis; myocarditis; post. sclerosis	0.073	0.088
12	S. L.	Chronic nephritis	0.060	—
13	R. B.	Nephritis; septicemia; sub-deltoid abscess	0.036	—
14	D. R.	Chronic nephritis	0.059	

Epilepsy. Boyd[23] found Fehling's test very positive in four epileptic insanities, while Thabius and Barbé[24] and Karpas[25] report negative results in their physicochemical studies in epilepsy.

These 14 cases were studied without regard to proximity of convulsions or of the type of the epilepsy. Half of the cases showed a moderate increase in reducing substance, the other half were normal, while the blood sugar concentration was slightly increased in 4 out of 6 cases (Table VIII).

TABLE VIII.—EPILEPSY.

Case.	Name.	Reducing substance.	Blood sugar.
1	J. H.	0.081	0.125
2	J. C.	0.067	
3	H. C. M.	0.093	0.100
4	E. McG.	0.094	0.118
5	L.	0.076	
6	G. H.	0.086	0.080 (vein)
7	McD.	0.063	0.063
8	M. G.	0.084	
9	M. A.	0.051	
10	E.	0.077	0.117
11	M. M.	0.100	
12	F. S.	0.066	
13	A. P.	0.074	
14	G. G.	0.084	

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[23] The Cerebrospinal Fluid in Certain Mental Conditions, Jour. Ment. Sci., 1912, No. 58, p. 203.

[24] La composition physico-chemeque du liquide céphalo-rachidien des epileptiques, Rev. Neurol. Jg., 1913, xxi, Nr. 17, S 248–253.

[25] Amer. Jour. Insanity, 1912–13, lxix, 143.

VARIOUS NERVOUS DISEASES. In a series of 33 cases of various mental and nervous disorders the only cases revealing abnormal figures were the hemiplegias, half of which were high, one case of hypomania also high, and one case each of melancholia and of suspected brain tumor, both of which were very low (Table IX).

TABLE IX.—NERVOUS DISEASES.

Case.	Name.	Diagnosis.	Reducing substance in spinal fluid.
1	G. F.	Hemiplegia	0.105
2	E. H.	Hemiplegia	0.073
3	L. B.	Hemiplegia	0.100
4	V. O.	Hemiplegia (arteriosclerotic)	0.092
5	F. M.	Hemiplegia	0.074
6	B. W.	Hemiplegia	0.086
7	McC.	Hemiplegia (cancer)	0.065
8	El.	Hemiplegia (cerebral hemorrhage)	0.078
9	Car	Subarachnoid hemorrhage	0.075
	"	" "	0.105
10	M. B.	Senile dementia	0.093
11	J. W.	Dementia precox	0.066
12	J. C.	Dementia; pneumonia	0.060
13	G. B.	Hypomania	0.171
14	Hb.	Brain tumor	0.081
15	A. C.	Brain tumor	0.061
16	J. U.	Brain tumor	0.070
17	R.	Brain tumor	0.071
18	V.	Tumor of cord	0.063
19	J. R.	Brain tumor	0.025
20	T.	Pituitary tumor (?)	0.074
21	N.	Optic atrophy	0.062
22	P.	Brain abscess	0.081
23	M. T.	Cord lesion	0.078
24	N. S.	Posterior sclerosis Nephritis; myocarditis	0.073
25	J. H.	Transverse myelitis	0.064
26	N. D.	Multiple sclerosis	0.074
27	Gr.	Primary lateral sclerosis	0.073
28	C. P.	Muscular sclerosis	0.078
29	P. C.	Progressive spinal muscular atrophy	0.067
30	C. A.	Idiot; castration	0.085
31	D. S.	Idiot; castration	0.087
32	V. N.	Sciatica	0.063
33	Wh.	Melancholia	0.048

SYPHILIS. The values here were so frequently low that they deserve attention (Table X), only 9 out of 29 cases falling within the normal limits. In 3 of the cases the blood sugar was normal, and it may be added that this is the only group of cases other than the meningitis series in which the sugar content of the fluid and blood did not usually run *pari passu*.

Kaplan[26] in a study of the differentiation of paresis and cerebrospinal syphilis found in untreated cases of general paresis that Fehling's reaction was always positive while in cerebrospinal syphilis it was sometimes absent. Here the increased protein content evidently influenced the reduction of the copper; under treatment, however, the reaction returned in the cases of cerebrospinal syphilis.

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[26] Laboratory Difference between General Paresis and Cerebrospinal Syphilis and Serology of Spinal Cord Tumors, Amer. Jour. Insanity, 1912–13, lxix, 336.

Shortly before the completion of this work an article was published by Biach, Kerl and Kabler[27] on the question of changes in the spinal fluid after the administration of neosalvarsan. These investigators also used Bang's method for determining the reducing substance.

TABLE X.—SYPHILIS.

Case.	Name.	Diagnosis.	Reducing substance.
1	M.	Tabes	0.071
	M.	Tabes	0.066
2	Tr.	Tabes	0.086
	Tr.	Tabes	0.064
3	I.H.	Tabes	0.069
4	Sp.	Tabes	0.049
5	McD.	Tabes	0.051
6	N.S.	Tabes	0.068
7	A. H.	Tabes	0.080
8	H. W.	Tabes	0.056
9	P. F. Y.	Tabes	0.044
10	Sh.	Tabes (?)	0.088
11	McL.	Tabes (?)	0.079
12	A. R.	Cerebral syphilis	0.052
13	Hor.	Cerebral syphilis	0.065
14	N. L.	Cerebral syphilis	0.038
15	G. G.	Cerebral syphilis (?)	0.084
16	Ne.	Cerebral syphilis (?)	0.055
17	E. A.	Bone lesions	0.083
18	J. J.	Periostitis	0.039
19	F. J.	Skin lesions	0.053
20	Wei.	Syphilis	0.068
21	N. H.	Syphilis	0.056
22	J. M.	Syphilis	0.052
23	Bl.	Syphilis	0.069
24	FO.	Syphilis (?)	0.056
25	Th.	Syphilis (?)	0.060
26	R. B.	Syphilis (?)	0.052
27	P. S.	Syphilis (congenital)	0.066
28	Ke.	Syphilis	0.038
	Ke.	Syphilis	0.042
29	Pr.	Syphilis (?)	0.053

Their series consisted of 14 untreated cases of syphilis, in which they found values varying from 0.04 to 0.09 per cent., and 12 cases treated with neosalvarsan with a resulting marked rise in the sugar content, one case reaching 0.34 per cent. Unfortunately the same patients were not used in studying the fluid before and after treatment, nor was the blood sugar estimated. They state that changes in the sugar content are not associated with any definite symptoms. As an explanation for the marked rise after the drug they suggest the possibility of renal impermeability and the fact that the neosalvarsan passes into the spinal fluid and is capable of reducing copper, and finally they quote Hess and Pohl, who believe that ferment action is responsible for the change as a result of destructive processes in the brain tissue.

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[27] Zur Kenntnis der Veränderungen der Spinal Flüssigkeit nach Neosalvarsan applikation, Wien. klin. Woch., 1914, No. 30, p. 1098.

This question will not be dealt with further, as investigations involving this and other phases of the fluid in syphilis are being carried out in conjunction with Drs. Laird and Jonas.

SUMMARY AND CONCLUSIONS. The consensus of opinion, based on recent literature, is that glucose is the principal reducing substance in the spinal fluid. Its concentration in health is slightly lower than that of the blood sugar, as shown by these studies in which Bang's method was used for both.

In meningitis there is the greatest disturbance in this relationship, there being a pronounced hyperglycemia associated with just as pronounced a drop in the sugar content of the fluid, this drop being due evidently to the destructive activity of the invading microorganisms.

In diabetes the sugar content of the spinal fluid is almost as high as that of the blood. In infections such as pneumonia there may be a hyperglycemia without apparent change in the spinal fluid. The reducing substance of the fluid is frequently increased in uremia, a condition, however, in which hyperglycemia also occurs.

A slight increase in the sugar concentration of both the blood and spinal fluid occurs in some cases of epilepsy, as it does in certain other nervous conditions, but the variety of cases observed in this series of 33 cases, and consequently the limited number of any one disease, renders inadequate any conclusion drawn at this time.

Syphilis frequently reveals lower figures than any other condition, with the exception of meningitis.

The micromethod for estimating the reducing substance of the spinal fluid has proved to be of value owing to its simplicity, reliability, and the small amount of fluid required.

Fehling's test is unreliable and misleading unless the proper dilutions are constantly used together with equal parts of the fluid and the solution. In the latter case fairly constant relative results are derived when there is a marked change in the amount of glucose and when there is not an excess of protein. Quantitative estimations of the glucose concentration of the spinal fluid are of distinct value from the standpoint of very early diagnosis and prognosis, especially in meningitis.

It remains for further investigations to reveal the value of this test in nervous disorders and syphilis.

I wish to express my thanks to the physicians and members of the resident staff of the University, Pennsylvania, Polyclinic, and Children's Hospitals, and especially to Dr. Rosenberger and Miss McNitt, of the Philadelphia General Hospital, for the contribution of the fluids examined.

TUBERCLE BACILLI NOT STAINABLE BY ZIEHL: THEIR CLINICAL SIGNIFICANCE.[1]

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In 1907 Hans Much published his original paper "Upon Gram-positive Forms of the Tubercle Bacillus, Not Demonstrable By Ziehl." Since that date his work and conclusions have been substantiated and confirmed by many other investigators. The importance of these findings, however, seems to have been appreciated chiefly abroad, and no such interest as they deserve has been aroused in this country. It has therefore seemed worth while to report upon a small series of cases studied by a modification of his method, with a brief review of the more important literature of the subject.

It is generally known and regretted that a considerable number of clinically suspicious or positive cases of tuberculosis of various organs cannot be bacteriologically proved, even after careful concentration of material and painstaking search for bacilli; it has also been recognized that in a certain number of such cases this material can infect the guinea-pig. Starting with the assumption, already considered by von Behring and others, that this discrepancy arises from the existence of a form of tubercle bacillus which does not take the Ziehl stain, Much[2] was able to demonstrate certain granules by the use of a modified Gram stain. These were small, round, blue-black bodies of varying size, sometimes showing a reddish tinge, sometimes isolated, frequently arranged in rows of from two to eight granules. These forms were found in the tubercles of a guinea-pig which had been injected with a culture of bovine tubercle bacilli, Ziehl organisms being undemonstrable. They were also present in the Ziehl-negative lung of a tuberculous calf. Pieces of this lung were incubated on serum tubes; after the third day the number of granules rapidly increased, and on the sixth day Ziehl-staining forms appeared. These results were confirmed on other animals. The pus from two cold abscesses was found to contain no Ziehl-staining organisms after prolonged search, but did contain numerous Gram-staining forms, and upon inoculation into guinea-pigs, produced typical tuberculosis, showing many Ziehl-positive bacilli. Much concluded that there is a form of tubercle bacillus not staining by Ziehl; that this form is a virulent but degenerated type, and that its staining properties are dependent upon different constituents than those which take the Ziehl stain.

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[1] This article was received for publication April 15, 1915.

[2] Beitr. z. klin. d. Tuberk., 1907, viii, 85.

These results and conclusions have been confirmed and extended by Much himself and by many others down to the present time. In 1908 Wirths[3] confirmed Much's original work in detail upon cases of human glandular tuberculosis and cold abscesses in which the Ziehl stain proved negative, the Gram stain positive, and the material infective to guinea-pigs. In these guinea-pigs he showed that the peritoneal exudate at first contained grandular forms, that these rapidly gave place to small Gram-staining bacilli, and these in turn to Ziehl-positive forms. Adding the pus from cold abscesses plus a culture of human bacilli to milk, he found that the Ziehl forms rapidly diminished or disappeared with a replacement by Gram-staining forms, and further noted that after a few days the Ziehl forms began to reappear. His conclusions entirely substantiated those of Much, and he considered a transition from one form to the other proved.

It is not necessary to note all the numerous reports scattered through the literature which confirm the general proposition that tubercle bacilli may be demonstrated by the modified Gram method in material in which no trace of them can be found by that of Ziehl. Certain of these reports, however, are of special interest as helping to clear up disputed points of etiology and diagnosis. In the field of dermatology, Lier[4] has found Gram forms present, and Ziehl forms absent in a small series of tuberculids and in lupus vulgaris. In 13 cases of the latter disease, Krüger[5] found only three positive by Ziehl, while Much forms were present in the lesions of all. Boas and Ditlevsen[6] among 20 such cases found Gram-staining forms in all, though only four were positive by the Ziehl stain. It is interesting to note in passing that the morphologically similar bacillus of leprosy also shows granular forms staining only by Gram, and that these have been found present where Ziehl-staining organisms failed.[7]

Weiss,[8] among eight cases of tuberculosis of the cervical, bronchial, and mesenteric glands, clinically and pathologically proved, was able to find no Ziehl-staining bacilli, though Much forms were present in all. The mesenteric lymph nodes of twenty-one children were examined by Wolff,[9] of which cases six were clinically and pathologically tuberculous. Of these six the lymph nodes in four were positive by Ziehl, in all by Gram. Of the remaining fifteen in whose glands there was neither macroscopically nor microscopically any suspicion of tuberculosis, Gram-staining Much organisms were found in three, in one of which, guinea-pig inoculation proved positive with the recovery of Ziehl-staining bacilli. This report is of special interest in view of the well-known periods of latency of tuberculosis.

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[3] Münch. med. Wchnschr., 1908, lv, 1687.

[4] Centralbl. f. Bakteriol., Orig., 1909, li, 678.

[5] Münch. med. Wchnschr., 1910, lvii, 1165.

[6] Berl. klin. Wchnschr., 1910, xlvii, 2106.

[7] Arning and Lewandowsky, Deutsch. med. Wchnschr., 1909, xxxv, 1225.

[8] Münch. med. Wchnschr., 1909, lvi, 443.

[9] Ibid., lvi, 2312.

Schottmüller and others[10] have reported the finding of Gram forms in the urine in tuberculosis of the urinary tract, although Ziehl forms were few or failed altogether. In the field of dentistry, Zilz[11] has contributed an interesting piece of work, finding and proving by guinea-pig inoculation the presence of granular forms of the tubercle bacillus in carious teeth. This is again of importance for the question of latent infections. In the field of ophthalmology, Wehrli[12] has found the granular forms of the bacillus in nodular keratitis, thereby confirming the previously suspected tuberculous nature of this lesion. The much disputed question of the frequency with which tubercle bacilli are found in the circulating blood has been studied from this new view-point. Jessen and Rabinowitsch[13] found in the blood of thirty-six patients the Gram-staining form nine times, the Ziehl seven. Sturm[14] in a series of pulmonary cases found the blood in 22 per cent. positive by Ziehl, in 42 per cent. by Gram, and in 46 per cent. positive by guinea-pig inoculation.

Fraenkel and Much[15] developed that phase of the subject which has aroused most widespread attention when, in 1910, they reported that there are present in the glands of Hodgkin's disease and of lymphatic leukemia structures which cannot be distinguished morphologically from those described by Much in tuberculosis. These observations have since been confirmed by other investigators and the organisms found further studied. Their exact relationship to the tubercle bacillus, whether an attenuated and culturally different type of it or whether only a more or less closely related organism, is not yet clear.

The relation of granular forms of the virus to pulmonary tuberculosis has, of course, not failed of investigation. Körber[16] examined the sputum in 167 cases of suspected pulmonary tuberculosis and found Ziehl-staining organisms in 54 per cent., Gram-staining forms in 64 per cent. Weirauch[17] reports the examination of fifty sputa of which 16 per cent. were positive by Ziehl in direct smears, 52 per cent. by Ziehl after antiformin concentration, and 72 per cent. positive by Much's modified Gram method. The antiformin treated sediment of one of these sputa, negative by Ziehl but positive by Gram, was injected into a guinea-pig which died forty-eight hours later of a thrombus. In this thrombus were found many short Ziehl-positive bacilli. Böhm[18] found among twelve Ziehl-negative sputa nine positive by the modified Gram method. Teleman[19] reported the presence of Gram forms in ten cases of lung tuberculosis, all of which were negative by Ziehl but positive on guinea-pig inoculation. An important piece of work is that contributed by Neumann and Matson,[20] who examined the sputum in forty-two cases of chronic lung disease. All were of long duration, with relapses, continued cough with considerable sputum; several were clinically "old-age emphysema," all were resistant to test tuberculin, but would clinically arouse suspicion of tuberculosis. In two of four tests the sputum proved infectious to guinea-pigs. Of this series all were negative by Ziehl; fourteen showed Much forms.

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[10] Münch. med. Wchnschr., 1908, lv, 2564; Leschke, Centralbl. f. Bakteriol., Orig., 1911, lix, 365.

[11] Beitr. z. klin. d. Tuberk., 1912, xxii, 97.

[12] Klin. Monatsbl. f. Augenh., September, 1909.

[13] Deutsch. med. Wchnschr., 1910, xxxvi, 1116.

[14] Beitr. z. Klin. d. Tuberk., 1911, xxi, 239.

[15] Münch. med. Wchnschr., 1910, lvii, 685.

[16] Deutsch. med. Wchnschr., 1912, xxxviii, 1494.

[17] Ztschr. f. Tuberk., 1909, xiv, 511.

While the great majority of reports substantially uphold Much's early conclusions as to the value of the method, opposition has not been wanting. It was early objected, with justice, that the presence of cocci in sputum and in other pathological specimens introduced a grave source of error through the readiness with which they might be confused with the somewhat similar granules. With the use of antiformin, by which all non-fast bacteria are dissolved while the resistant granules remain intact, this argument has entirely lost its force. A second objection is found in the papers of a series of men who sought to show that the Gram stain demonstrates no more bacilli than does the Ziehl. This objection, as Much justly observes, entirely misses the point of the matter, for the value of his method lies not in the relative number of bacilli shown in a given specimen, but in the fact that the Gram stain not infrequently shows the presence of the granular forms in specimens in which no Ziehl forms at all are to be found. The most determined opposition has arisen from Spengler and his school, who do not deny that there is a form of tubercle bacillus not demonstrable by Ziehl, but insist that Much's granular forms and Spengler's "splitters" are identical, that Much has simply stained these structures in a new way and deserves no credit for their demonstration. The discussion need not be entered upon here, being largely theoretical, chiefly turned upon the question of priority and somewhat embittered; it is sufficient to say that the balance of evidence supports the view that granules and "splitters" are not identical and that Much deserves all credit for his discovery.

The biological relationship of Much forms to Ziehl-staining forms of the tubercle bacillus is a matter of considerable interest. They may be considered as a natural stage in the evolution of the bacillus, as the result of degenerative changes, or may be classed as spores (*i. e.*, as resisting forms). The evidence which has accumulated tends

[18] Centralbl. f. Bakteriol., Orig., 1911, lxii, 497.

[19] Deutsch. med. Wchnschr., 1910, xxxvi, 891.

[20] Beitr. z. Klin. d. Tuberk., 1912, xxiv, 193.

to show that they are predominantly found in tissues of a distinctly fibroid character, in old cavities, in the pus of cold abscesses, in old cultures, in the notably indolent lupus lesions, and in sclerosed lymph glands—facts which, taken together, mark them as forms assumed under unfavorable conditions, whether they be the result of sporulation or of degeneration. The same conclusion is suggested by observations that under favorable cultural conditions they are rapidly replaced by Ziehl-staining forms. In this connection the work of Wirths noted above is of interest. His experiment is further supported by one of Much's, who incubated pus from a renal abscess, in which microscopically only granular forms could be seen, in Heyden bouillon, and after five days found Ziehl-positive bacilli in pure culture. He further added a Ziehl-positive culture of bovine bacilli to the perhydrase treated milk of a tuberculous cow and found that the Ziehl forms gradually diminished and disappeared. When glycerin was added to a portion of this culture, Ziehl-positive forms promptly reappeared.[21] Against their classification as spores in the commonly accepted sense is the fact that the granular forms are rather less resistant to the action of antiformin than are the Ziehl forms; their resistance to other chemical and physical agents has not yet been reported upon. It is of interest to note here that the granular forms appear more frequently in the bovine than in the human type of bacillus.

Closely allied to the problem of their biological relationship is that of the chemical relation between Ziehl and Much forms. Here the views of Deycke and Much are probably correct. Starting with the fact that the Ziehl-staining property is dependent upon the fatty acid component of the bacillus, they believe that a progressive loss of this substance coincides with a progressive diminution in the intensity and uniformity of the Ziehl stain; with its complete loss the bacillus no longer stains at all by Ziehl. There remains, however, a substance capable of taking the Gram stain, probably a proteid. This material is impregnated with the neutral fat component which serves to protect it in some degree against the stain, accounting not only for the slowness with which this acts, but also for the fact that Much forms, unlike other bacteria of protein composition, are antiformin-fast. In support of this view, Deycke and Much[22] planned experiments with the action of neurin and other solvents upon masses of tubercle bacilli, and found that by increasing the action time of such solvents the Ziehl stain could be made to become progressively weaker, Gram forms replacing Ziehl forms. These were in turn replaced by a homogeneous mass, at first staining by Gram, later failing to take any stain. According to this view the loss of fatty acid is a degenerative change, brought about by the protective forces of the body, or, as in the centre of caseous lesions, by a possible deficiency in nutriment. Matson has suggested that the fat-splitting ferments of the lymphocytes play a prominent part in the removal of fatty acid and that the proteolytic ferments of the leukocytes are very possibly responsible for the final degeneration of the granules themselves.

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[21] H. Much, Berl. klin. Wchnschr., 1908, xlv, 691.

[22] Münch. med. Wchnschr., 1909, lvi, 1985; ibid., 1910, lvii, 633.

The investigations to be here reported comprise forty-six sputum examinations upon forty-four patients, in all of whom lesions of the lung or of the bronchial or mediastinal glands were clinically present or suspected, but whose sputum on direct examination contained no tubercle bacilli. Many known positive sputa were also examined by this method; all contained many Gram-staining as well as Ziehl-staining forms. Where possible, two or three ounces of sputum has been used, otherwise the entire twenty-four expectoration. A direct smear was in all cases first examined by the usual Ziehl-Nielsen stain. The sputum was then concentrated by the modified Ellerman-Erlandsen method as follows: an equal amount of 0.6 per cent. sodium carbonate was added, the whole thoroughly shaken and allowed to stand at 37° C. for twenty-four hours; if complete homogenization had not occurred the time was extended to forty-eight hours. This mixture was then centrifuged five minutes at high speed and to the sediment an equal amount of 30 per cent. antiformin added. Digestion was allowed to proceed for twenty minutes, the mixture again centrifuged, the sediment washed with water to remove excess of antiformin, again centrifuged, and smears made from the resulting sediment. In searching for Much forms the so-called "double stain" of Weiss was used. This consists of three parts of ordinary carbol fuchsin solution to one part of a carbol methyl violet solution, the latter prepared by adding nine parts of 2 per cent. carbolic water to one part of a saturated alcoholic solution of methyl violet. This stain is useful for about two weeks if not exposed to the air or to direct sunlight; after this time a precipitate forms rendering it useless.

The technique found to give the most satisfactory results is as follows: the smear is immersed in the stain for forty-eight hours at room temperature, washed gently, covered with Gram's iodin solution for five minutes, being brought to gentle steaming, decolorized with 5 per cent. nitric acid for one minute, 3 per cent. hydrochloric for ten seconds, and washed with a solution of equal parts of acetone and 95 per cent. alcohol until no more color is removed. After drying the smear is ready for examination. No counterstain was used, as it was found that this added nothing to the ease of search and could at times prove confusing. Many modifications of this method were tried, including a quick method, in which steaming replaced the forty-eight-hour exposure to the stain, the use of a twenty-four-hour exposure, the effect of longer staining in the cold, and the relative value of I. K. I. and Lugol's solution as a mordant. The above outlined method was found to give the most clear-cut and reliable preparations, and all results were based upon it. In addition to a direct smear, a smear of the concentrated sputum was in each case examined by the Ziehl stain to serve as a control for the presence of Ziehl-staining bacilli in the antiformin concentrated sputum, and for the presence of undigested cocci which might prove a source of confusion with the Much granules. In several instances cocci were thus recognizable, and such preparations are omitted from consideration. Twenty minutes' search of a good preparation, using a mechanical stage, has been taken as a standard before either direct smears, concentrated sputum, or Much-Weiss preparations have been recorded as negative.

With this method the granules appear as small, round, sometimes slightly ovoid bodies, frequently refractile, varying somewhat in size from a half to three-quarters the size of a staphylococcus, *i. e.*, about 0.4 to 0.5 microns in diameter. In color they are of a blue- or violet-black, with sometimes a faint tinge of red. They may occur singly, sometimes in small groups, but are more often arranged in chains of from two to eight granules, usually of not more than four. The granules thus arranged in chains usually, but not always, show a faintly bluish tinged substance connecting them; this bacillus body may have a faint or a marked red tinge. In other instances isolated granules may show a delicate red halo or a faintly reddish prolongation. These various figures may all be found in known Ziehl-positive sputa, and the intermediate forms from the small isolated granule on the one hand to the solidly red bacillus on the other may be readily traced. Having regard to the somewhat remote possibility of confusion with cocci, only those preparations have been recorded as positive in which the granules either appeared in characteristic chains with a connecting substance between or showed a definite reddish prolongation.

The cases studied group themselves clinically into three rather distinct classes. First are those in which the tubercle bacillus has at some time been demonstrated, but has since disappeared coincidently with clinical healing. Of these some have at the time of examination complained of symptoms suggesting a recrudescence of the old process; others have been subjectively and clinically well, save for slight occasional expectoration. In this group are comprised nine patients in whom the results were as follows:

	Positive.	Negative.	Per cent. Positive.
Ziehl (direct smear)	0	9	0
Ziehl (concentrated sediment) . . .	1	8	11
Much-Weiss method	6	3	66

A second group comprises those cases in which signs and symptoms warrant the suspicion of an early or of a mild, longer continued tuberculous process in lung or mediastinum, but which have shown a persistently negative sputum. Fifteen cases are included in this group, among whom the results were as follows:

	Positive.	Negative.	Per cent. Positive.
Ziehl (direct smear)	0	15	0
Ziehl (concentrated sediment) . . .	2	13	13
Much-Weiss method	11	4	73

The largest and most important group comprises those cases in which the clinical picture is that of long-standing cough with more or less profuse expectoration, subject to exacerbations and remissions, occasional manifestations of a mild toxic absorption, and upon physical examination, signs, sometimes of a fibroid process of varying extent, sometimes of bronchiectasis, sometimes of chronic bronchitis or emphysema. Occasionally there are signs suggesting glandular enlargement in the mediastinum or root of the lung with an otherwise negative chest. Here too are included several cases of recurring asthmatic attacks without other symptoms. A few of this group are reported to have shown tubercle bacilli at one time or another, some have undergone sputum examinations extending over many years with no positive result. Among this group the results are as follows in twenty-two examinations:

	Positive.	Negative.	Per cent. Positive.
Ziehl (direct smear)	0	22	0
Ziehl (concentrated sediment) . . .	2	20	9
Much-Weiss method	18	4	82

In addition, one specimen of chest fluid from a patient with frank lung tuberculosis has been found to contain Gram-staining forms though no Ziehl-staining organisms could be demonstrated. Also, the urine from a patient with clinically undoubted tuberculosis of the bladder contained rather numerous Gram forms, though the Ziehl stain gave entirely negative results.

If the results in these three groups be added together, it will be found that of the 46 examinations 5, or a little over 10 per cent., were positive for Ziehl-staining organisms in the antiformin concentrated sputum, while 35, or about 76 per cent., showed Gram-staining forms. The preponderance of sputa containing Much forms in Groups II and III seems especially significant upon the supposition that this type represents a resistance form of low virulence. The individuals of the latter group were nearly all leading rather active normal lives, and were not seriously inconvenienced by the cough, slight shortness of breath, recurrent asthmatic attacks, frequent attacks of acute bronchitis, or mild toxic symptoms for which they presented themselves. The results in this group are further of considerable significance for the prophylaxis and prevention of tuberculosis. The readiness and rapidity with which these granular, Gram-staining forms may, under favorable conditions, transform themselves into virulent Ziehl-staining bacilli has been proved by the work of Much, Wirths, and others as noted above. If now these forms are present in the background of some proportion of cases of chronic bronchitis, old age emphysema, recurring asthmatic attacks, and other chronic lung conditions in which there seems no reason for suspecting tuberculosis, and so for enforcing proper care of the sputum, it is not hard to believe that such cases may be a really important factor in the spread of tuberculosis.

The individuals in these groups represent common types of patients in whom the problems of diagnosis or of management may be puzzling. In the first group this uncertainty presents itself in the necessity of deciding whether a slight occasional expectoration or a tendency to frequent colds with accompanying expectoration, in the presence of otherwise entirely negative findings, is to be regarded as significant of continued active infection. In the second group there arises the question whether trifling or obscure symptoms and physical signs have anything to do with tuberculosis; upon a correct decision depend most important questions of management. The widely varying clinical pictures of the third group may suggest equally various possible etiologies, of which a latent tuberculosis may appear the least probable.

In conclusion, it may be said that this work, undertaken with some skepticism, has resulted in the conviction that the granular forms described must be regarded as identical, for diagnostic purposes, with the ordinary Ziehl-staining form. In any patient suspected of tuberculosis in whom Ziehl forms cannot be demonstrated, it is as important to search for Gram-staining forms as it was for the Ziehl-staining bacilli, and a diagnosis of tuberculosis cannot be certainly excluded until such search has proved negative. The type of case in which they are characteristically present strongly supports the conception that they represent a resistance stage of low virulence, and their presence alone warrants a much more favorable prognosis than does the presence of Ziehl forms. Further, they are probably a definite factor, of as yet undetermined importance, in the spread of tuberculosis.

I wish to thank cordially Doctor Carroll E. Edson for the privilege of studying many of these cases and for much kind assistance in the work.

The following histories of patients showing Much forms are appended as typical of those cases which have been grouped in each of the three classes above noted.

Group I. H. B., a single man, aged twenty-three years, has had since he was twelve years old two or three asthmatic attacks a year, coming usually in winter, lasting three or four weeks. There have been no attacks for the past three years, but he has had several severe colds each winter. In the spring of 1912 he began to "run down," was tired, with not much loss of weight. Cough began in July with a little yellow expectoration. Tubercle bacilli were found in September, 1912. At this time he had dulness, increased fremitus and whisper, prolonged breathing, and a few rales after cough at both apices in front. No fever.

Under rest for four months the cough and expectoration entirely ceased, the rales disappeared, and in six months he took up active business. In September, 1913, he took a three days' trip, involving laborious mountain climbing, without apparent ill effect.

During January and February, 1914, he had a succession of severe colds, with temperature, cough, sweating, and much loose expectoration. When seen in April he had occasional cough, with slight white expectoration. No signs of activity could be detected in the lungs; he was afebrile and his general condition was excellent. At this time the sputum was negative to Ziehl, both in direct smear and in the concentrated sputum, but positive by the Much-Weiss method, showing many scattered granules and occasional chains of two or three. Both cough and sputum have since entirely disappeared.

Group II. Mrs. J. F., aged thirty-two years, had, in September, 1912, a bronchopneumonia in the left lower lobe, and was in bed five weeks. This was followed by a dry pleurisy on the right side. Since then there has been a persistent cough, with a little morning expectoration (January, 1914). She has had several mild attacks of bronchitis this winter with increased cough and expectoration. There has been one negative sputum examination. She was at this time twenty-five pounds below weight, very nervous; the pulse was 100 to 110, with no elevation of temperature. There was occasional pain under the sternum without relation to food or exertion, and no other symptoms.

Chest examination showed slight dulness in the right mid-back from the fourth to the eighth rib inside the scapula, without change in voice or respiration. No rales. The chest was otherwise entirely negative. The Roentgen-ray gave a definitely enlarged bronchial gland shadow corresponding to the area of dulness. Sputum examination was negative for Ziehl-staining forms in both direct smears and concentrated sediment. By the Much-Weiss method there were present chains of two and three granules, and occasional granules showing definite reddish prolongations.

Under rest and forced feeding the patient has gained weight and is less nervous; the substernal distress has disappeared, cough and sputum have gone, and she feels well. The chest examination remains the same.

Group III. C. R. R., a widower, aged forty years. One brother died of tuberculosis ten years ago. The patient had pneumonia twenty years ago. In 1907 he had an acute appendicitis, with operation, and has never regained his full strength. Sometime during that year he began to have considerable cough and expectoration, which has continued since. In December, 1909, he was in bed for a month with a "heavy cold," having much cough, fever, and sweats. In the spring of 1910 he had blood in the sputum, with a great deal of pleural pain in the right lower axilla. Sputum examination was negative for tubercle bacilli. The chest in January, 1911, showed exaggerated breathing at the right apex, with feeble breathing and a few moist rales in the right lower axilla.

From this time until seen in January, 1914, he has had continuous cough, with from a quarter to two ounces of yellow sputum a day; occasionally this has been blood-stained. He has had numerous acute flare-ups with fever, lasting one to three weeks, and has complained at various times of considerable muscular and joint aching. The chest has repeatedly shown rales at one or both apices, above and below the clavicles, and in the right lower axilla, but on the whole there has been little permanent extension of involvement. Repeated sputum examinations have been negative for tubercle bacilli. He has continued an active business life.

Sputum examination in January, 1914, showed no Ziehl-staining organisms either in direct smears or in concentrated sediment. In the Much preparations there were present very many granules, arranged both in short chains of two and three and in long chains of four, five, and six granules.

Since this time his general condition and symptoms have remained much the same. A further sputum examination has not been possible.

HODGKIN'S DISEASE: A STUDY OF A SERIES OF TWENTY-FIVE CASES.

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(From the Pathological Laboratory of The Roosevelt Hospital.)

In the past five years we have had at the hospital 23 cases of Hodgkin's disease; 6 were females and 17 males; of the latter 1 was a negro. This gives a ratio of 1 female to 2.8 males, but the admission proportion to this hospital is 1 female to 1.7 males. Considering this from our experience, it is relatively and absolutely more common in men than in women. Reed's[1] series gave 7 males to 1 female, and Bunting,[2] in two series, gives 15 to 10 and 15 to 13. Clark[3] refers to a series of 43, 37 of which were in men, and Ziegler, 149 males and 71 females. Roughly this shows it to be about twice as common in men as in women.

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[1] Johns Hopkins Hosp. Report, 1902.

[2] Johns Hopkins Hosp. Bull., 1914, xxv, 173.

Thirteen of the cases occurred in the third and fourth decades, and four each in the first and second. We are unable to make the distinction referred to by Bunting of the majority of males being under 34 and that of females being over 33. It is generally accepted as a disease of youth and early adult life, with occasional cases at both extremes. Ziegler gives 45 per cent. of cases between 21 and 40.

The primary foci have been, as far as observation permits, cervical 13 (left 7, right 4, undetermined 2), axillary 3, retroperitoneal 3, right femoral 1, intestinal 1, and undetermined 2. Of the latter the first lesion noted was the skin, but we do not consider this as primary. Practically all writers agree to a primary cervical involvement in the majority of cases, and suggest the mouth, gums, tonsils, nose, and accessory sinuses as the portal of entry of the infecting agent. Reed[4] considered all cases of this origin, saying that no case had been described in sufficient detail to permit of a positive statement that the disease started elsewhere. We have had one case of primary intestinal origin, and Bunting[5] details a case of inguinal involvement following a cystitis. Three of the cases were diagnosed following operation and removal of retroperitoneal tissue. These cases are, in all probability, of primary intestinal origin. In only two of our cases (5 and 16) has the onset been definitely traced to previous infections, and both of these were from the throat, tonsillitis, and diphtheria.

The following cases are cited from Ziegler's[6] series of 220 cases. Primary cervical involvement 50 per cent., supraclavicular and submaxillary 6 per cent., axillary 10 per cent., mediastinal and inguinal 3 per cent., spleen 9 per cent., and retroperitoneal 10 per cent.

It is found more commonly in the lower classes, but that it is quite cosmopolitan in its tendencies is shown by the fact that eight countries are representated in this short series.

The time elapsed between the first sign of the disease and consultation has varied from a few weeks to ten years, with an average of ten months. The following are given as the reasons for consultation:

1. Tumor alone, 14.
2. Pain alone, 4 (epigastric, 1; right, lower abdomen, 2; right arm, 1).
3. Tumor and pain, 2.
4. Chills and fever, 2.
5. General weakness, 1.

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[3] British Med. Jour., 1901, ii, 701.

[4] Loc. cit.

[5] Loc. cit.

[6] Die Hodgkinische Krankheit, Jena, 1911.

Eight of the cases were without symptoms throughout the observed course, but all of these with one exception were under six months' duration; of the remaining 15 cases, 5 complained of pressure pain, 4 abdominal pain, obstruction, gastric ulcer, and appendicitis, and 2 of general body pain. It is to be regretted that we did not have autopsies in more cases, but particularly in Case 20, who suffered severe pain in the back and bones, to determine a possible relation to myeloma or myeloblastic pseudoleukemia of Sternberg.[7]

The other prominent subjective symptoms were general weakness and chills and fever in 6 cases, loss of weight in 8, profuse night sweats in 4, pallor in 2, pruritus in 2, toxic vomiting and jaundice each 1. One writer[8] refers to prurigo exantheme as a frequent early symptom, in one case having been present for three years before the development of glands. In only two of the cases did such symptoms appear before one year, and in one of the cases chills, fever, and sweats were the first symptoms; Cases 14 and 15 developed such two months after onset.[9] Both these cases left the hospital against advice in very poor condition, the former with a temperature of 105°, the latter 103°, and lived only a short time. In the other cases such symptoms developed after one year. We consider from a clinical stand-point two types, symptomatic and latent.

Symptomatic Type. (*a*) acute, 3 cases; (*b*) chronic, 18 cases.

(*a*) Symptomatic Hodgkin's disease, as will be seen from the analysis, might be classified as acute and chronic. The former gives a distinct picture of acute toxemia, simulating typhoid, sepsis, or malaria, and runs its course in a few weeks to six to eight months, with progressive loss of weight, general weakness, chills and fever, night sweats, and sometimes vomiting. We have had three cases of this type, 10, 14, 15. Osler[10] believed that such reactions were probably due to an intercurrent infection.

Such cases are those reported by Karsner,[11] Chark,[12] Hirschfield, and Isaac.[13] In the latter cases a description of one of the glands suggests that it was probably longer than six weeks' duration, and of the type described in the next group. As the course of this case was so acute, I will detail a brief *résumé*. The patient, age sixty-one years, gave a history of swelling of the back of neck, of four weeks' duration, followed shortly by marked weakness, swelling of feet, and difficulty in breathing. The left cervical, right supraclavicular, and both axillary groups were moderately enlarged. The temperature was 101.4° to 103.6° F.

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[7] Verhandl. d. deutsch. path. Gesellsch., 1912.

[8] Pathologie d. primarer Krankungen des Lymphatischen and hematopötischen Apparates, 1915.

[9] Ziegler, Loc. cit.

[10] Practice of Medicine, New York, 1907.

[11] Arch. Int. Med., 1910, iv, 175.

[12] British Med. Jour. 1901, No. 2, p. 701.

[13] Med. Klinik., 1907, lii, No. 52.

The blood findings changed in two weeks from Hb. 20 per cent., red blood cells 2,290,000, white blood cells 24,000, to Hb. 15 per cent., red blood cells 1,190,000, white blood cells 20,000. In six weeks from the onset of the swelling the patient died, running a subnormal temperature for several days before death. Ziegler[14] cites a case of a few weeks' duration, and one very suspicious case acutely toxic of but a few days' duration.

(*b*) By the chronic cases we refer to those of long duration, characterized by exacerbation and remissions. These cases we find to be of more than a year's duration, and many under better hygienic conditions, excision of active foci, hospital routine, and Roentgen-rays improve remarkably for certain periods, but the time comes when all these measures fail. The subjects pass into a state which characterizes the acute cases, the picture of acute toxemia develops with high intermittent fever, which becomes subnormal a few days before death.

Case 6 appears as a good illustration of the effects of energetic Roentgen-ray treatment, the exacerbations and remissions clinically and subjectively, but with progressive lymphatic enlargement. All but five of the cases appear as this type.

LATENT TYPE. Two cases.

The latent type manifests itself in a prolonged course over a period of years, with little if any subjective symptoms, save those referable to the local disturbance, absence of fever, chills and sweats, but characterized by pathological exacerbations in that the glands alternately increase and decrease in size. As an example *par excellence* of this variety we offer Case 24, of twenty-five years' duration. Nowhere in the literature have I been able to find a case which approaches this in duration; the longest was a case of seventeen years. This man, with the exception of the disfiguration, appears in perfect health. A second case, 23, stands as another example. Of these cases the latter gives a typical pathological picture, but the picture of the former is masked by fibrosis. This type of case is of rare occurrence; by far the larger majority of cases come under the heading chronic symptomatic; that is, the type of case which, according to Reed, Bunting, and others, runs its course in from three to five years.

Many writers have attempted to designate Hodgkin's disease from the tissue or location in which it develops, calling it abdominal, splenic, hepatic, or lymphatic; but this classification is to be discouraged, as it is a systemic disorder, with marked local manifestations. Sternberg[15] advises the term pseudoleukemia for the groups lymphosarcoma, lymphogranuloma, and plasmoma, diseases with hyperplasia of lymphoid without leukemic blood findings, and speaks of an analogous disease of myeloid tissues,

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[14] Loc. cit.

[15] Verhandl. d. deutsch. path. Gesellsch., 1912, p. 22; ibid.

"myelogenous pseudoleukemia." In contrast to this teaching, however, are the cases of Symmers[16] and Ziegler[17] of solitary splenic involvement.

The spleen was involved in seven of the cases, the liver in four, and the lungs and kidney in the case with autopsy. At the present time one of the patients has a diffuse infiltration of the left breast and a few nodules in the right. The above figures are certainly low, for the majority of the cases were seen in the first year. Could we have seen them at later dates our figures might nearer approach Clark's[18] as in half of his cases an enlarged spleen was noted, while Ziegler gives 65 to 75 per cent. of cases with splenomegaly. The involvement of internal organs is merely a question of time, and though a disease primarily selectively lymphatic, it causes a compensatory lymphogenesis in other organs with subsequent involvement. It is on account of this fact that Hodgkin's disease has been considered in the light of a new growth, but for late years there has been a tendency toward the opinion that it is of an inflammatory nature, occasionally showing malignant transformation. Tusnoda[19] is of the opinion that it is primarily a malignant tumor of lymphoid elements, with the inflammation as a matter of secondary importance. Dietrich[20] believes it to be a granulomatous lymphosarcoma. Symmers,[21] Harsner,[22] Yamasaki,[23] and

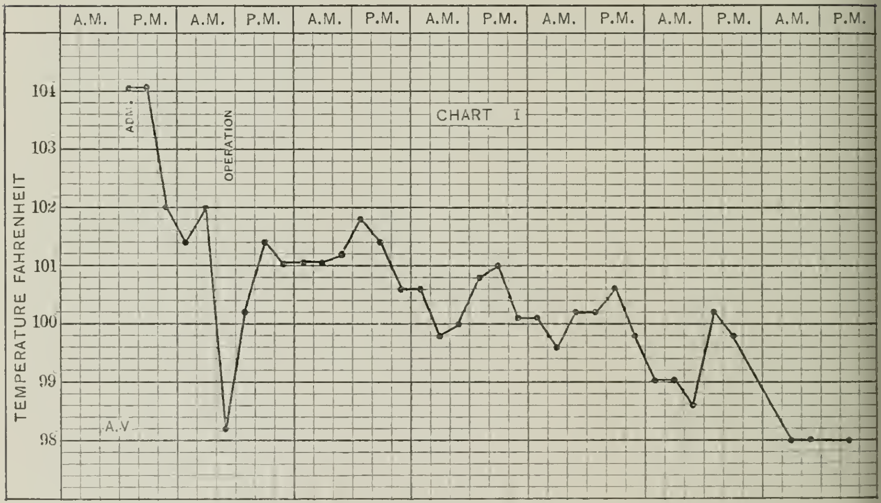

Chart I

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[16] Arch. Int. Med., 1909, iv, 218.
[17] Loc. cit.
[18] Loc. cit.
[19] Virchows Archiv, Band cciv, 265.
[20] Deutsch. med. Wchnschr., 1908, Heft. 27.
[21] Loc. cit.
[22] Loc. cit.
[23] Ztschr. f. Heilk. 1904, xxv, 269.

and Hirschfield,[24] are of the opinion that it is primarily Hodgkin's, but may undergo malignant transformation.

The Wassermann reaction was made in seven cases and was found negative in each instance.

TEMPERATURE. In thirteen of the cases the temperature was normal during observed course. It does not seem to be entirely dependent upon the duration of disease and the extent of involvement, but upon some factor which at present we are unable to reckon with. The duration varied in afebrile cases from two months to twenty-five years, but the larger percentage averaged about six months. This coincides with the absence of other clinical symptoms which, as we have seen, occur in the majority of cases after six months. The extent of involvement in these non-febrile cases was as follows: unilateral cervical 5, general glandular 2, retroperitoneal 2, femoral 1, and general glandular with enlargement of liver and spleen 1.

The cases we have had an opportunity to observe for much longer periods are those clinically ill with all the signs of an acute infection with a very variable temperature. Here the duration is seen to be of more than seven months in the majority of the cases. The known involvement in these cases was bilateral axillary and cervical 2, bilateral cervical 1, retroperitoneal 2, general glandular 1, cervical and spleen 1, and extensive glandular and visceral 1. Considering these cases individually, many similar cases will be found in the foregoing group. This fact is certainly a strengthening link in the infectious theory.

From a study of the temperature charts of these cases the striking feature is the extreme irregularity of the temperature wave. There is no set type for any one case, for all the classical curves, of tuberculosis, typhoid, sepsis, and malaria, are simulated, the tuberculous type perhaps being more often seen. No two charts resemble one another. One case, Chart I, with early retroperitoneal involvement, was admitted to hospital with a temperature of 104° and a suspicious history of acute appendicitis. At operation the appendix was found to be normal but about the cecum was a rather extensive glandular enlargement, a small portion of which was excised for diagnosis. The temperature gradually descended to normal on the sixth day, and remained so.

Another case, Chart II, with a history of several months of attacks of fever, chills, and sweats, was admitted to hospital, and for nine days temperature was normal. It then rose in twenty-four hours to 102.6°, with a morning drop to 99° to 103.6° and 104° on the two following days. For six days it again remained normal, with gradual rise to 104°, oscillating between 101° and 105° for five days, and continuous 104° to 105° for three days, when the patient left the hospital against advice and has not been heard from since. This is the best example we have had of the so-called Pel Ebstein recurring fever. This type of fever, according to Fabian,[25] occurs in about 50 per cent. of cases, and is seen in other conditions, such as carcinoma of internal organs. The same writer quotes Gowers, finding it in two-thirds of cases. According to Zeigler it occurred but eight times in a series of 220 cases.

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[24] Folia Hemat., 1910, x, 67.

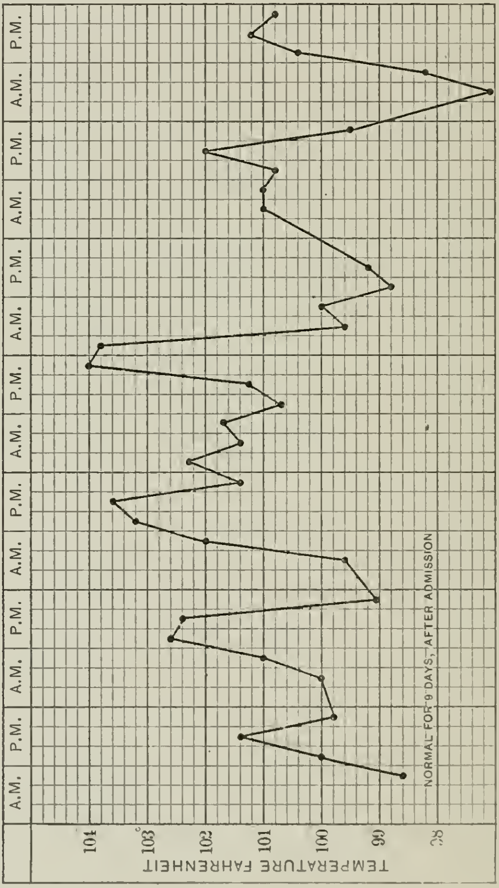

CHART II

Chart III is that of a boy, aged nine years, who a year previous, with extensive cervical involvement, had a normal temperature through six weeks' observation. The reaction as seen in the chart was followed for nine weeks by practically a normal temperature. One year later temperature for eleven weeks was very irregular,

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[25] Centralbl. f. Allg. Path., 1911, xxii, 145.

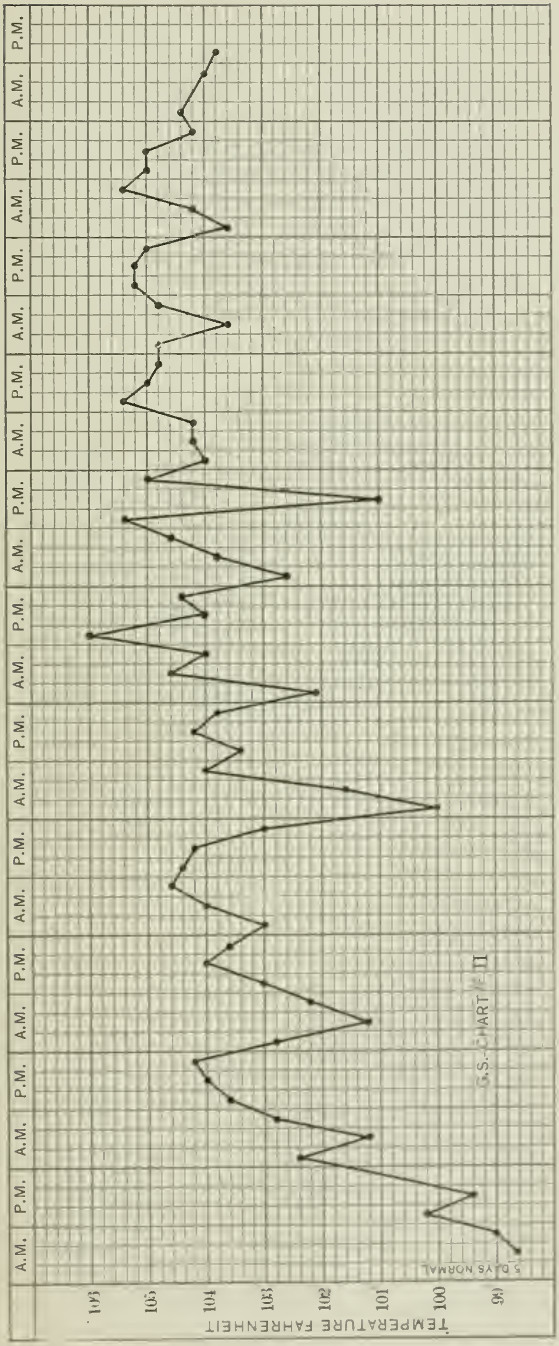

Chart II (Continued).

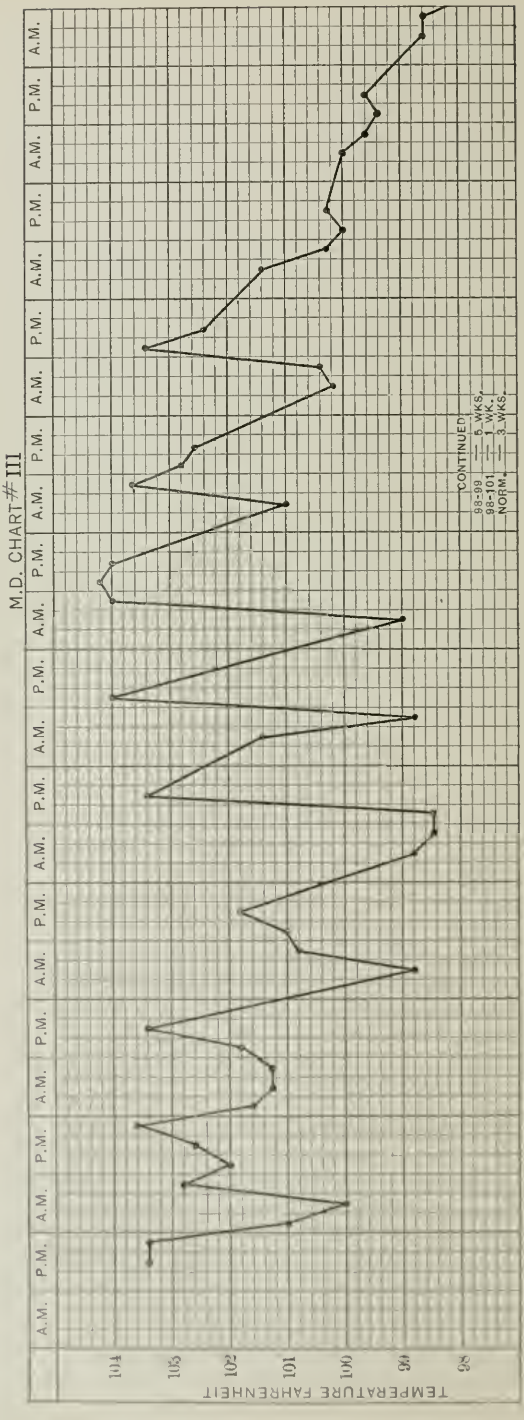
M.D. CHART # III
A.M.
P.M.
104
103
102
101
100
99
98
TEMPERATURE FAHRENHEIT
CONTINUED
98-99 5 WKS.
98-101 1 WK.
NORM. 3 WKS.

Chart III

98°, 101°, 102°, with evening elevations, it being normal for one week before death.

The course represented in Chart IV is that of a female, aged twenty-four years, with an extensive cervical and axillary involvement. This was followed by periods of 99° to 101°, occasionally to 103°, but for three weeks before death was frequently subnormal. A case very similar but with more extensive axillary involvement for one week gave a temperature of 99° to 101°. Temperature taken frequently since has been normal. In the former case (Chart IV) the lungs, spleen, and kidneys were involved; in the latter case the left breast is diffusely hard and infiltrated, but there is no evidence of visceral disturbance.

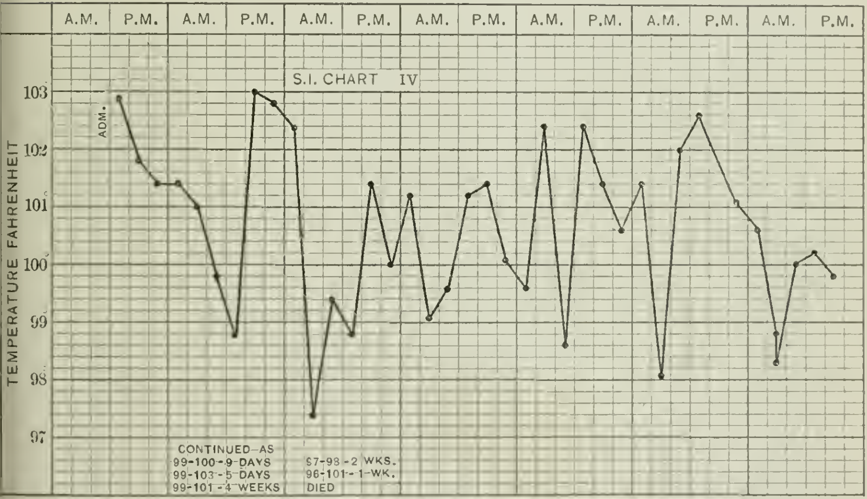

Chart IV

Why one case with a slight involvement and another case with an extensive involvement should show such diversity in toxicity and clinical findings could perhaps be best explained on the infectious theory. During the febrile attacks there is apparently no change in the pathology of the disease, but Zeigler suggests that these reactions are due to metastases to internal organs.

In five of the active febrile cases blood cultures were taken and were all reported negative. If the organism described as the etiology is responsible, no better cases could be obtained to rule out at least a septicemia. These cultures were made on the ordinary laboratory media grown aërobically. With the now improved technique along these lines and with enriched media, if there is an associated septicemia, it will not be long before it is worked out.

Physical Status. Seven of these patients were in good general physical health, showing nothing of importance except local conditions. In these the average duration of the disease was five months.

The most common physical signs exclusive of the specific trouble are referred to the lungs, *i. e.*, a few cases of marked recurring hydrothorax. One case was tapped six times and a cloudy straw- to amber-colored fluid obtained, showing 97 per cent. lymphocytes and 40 per cent. by volume of albumin; at the autopsy the lungs presented an extensive process of Hodgkin's disease. In another case the fluid obtained was of a greenish, milky color, with 400 cells per cm.; polynuclears 32 per cent., lymphocytes 68 per cent., pseudochylous fluid. A third patient whose sputum was negative for tubercle bacilli on four examinations, was tapped eleven times, the fluid varying from a light amber to a dark brown, containing few cells and 1.5 per cent. of albumin. The fluid is not diagnostic, as it closely resembles that seen in the exudation of tuberculosis. Two other cases gave signs of a dry pleurisy at the base, and one, suspicious signs of tuberculosis at the left apex.

Five of the cases showed markedly hypertrophied tonsils, and from these were elicited frequent attacks of tonsillitis. In two others the teeth and gums were in very poor condition. Pyorrhea in one case and a protracted stomatitis in another had been very troublesome.

In this connection it seems appropriate to refer to some recent work done on the bacteriology of cervical glands. From three cases of tuberculous lymphadenitis, one case of large round-cell sarcoma (primary mediastinal), one case of Hodgkin's disease, and one gland diagnosed by Bunting as a typical Hodgkin's picture, but by Warren, Mann, Butterfield, and the writer as a peculiar metaplasia, a diphtheroid organism has been obtained, closely related to, if not identical with, the so-called B. hodgkini of Negri and Miermet,[26] Fraenkel,[27] Bunting,[28] and others. A gland from an active Hodgkin's disease planted on favorable media, such as Dorsett's egg and glycerine phosphate potato agar, after three weeks' observation is still sterile. We are inclined to believe that this organism is not the specific cause.

The Present Status. The present status of the cases is as follows: 7 have died, 2 of these directly following operation, 1 of which died with the picture of acute toxemia. This case at operation presented two large retroperitoneal masses, and a section was removed for diagnosis. Patient returned to ward in good condition, but a few hours later was taken with a shaking chill, temperature 104°, and frequent projectile vomiting. The following day temperature rose to 105.6°, followed by chill, collapse, and death. It was suggested at the time that operative interference may have liberated an excess of toxin, producing a condition analogous to postoperative thyrotoxicosis. The average duration of life in the other 5 cases was two and a half years, the longest being two years and eleven months and the shortest eight months.

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[26] Centralbl. f. Bakteriol., 1913, lxviii, 292.

[27] Münch. med. Wchnschr., 1910, lviii, 655.

[28] Arch. Int. Med., 1913, xv, 236; Jour. Amer. Med. Assoc., 1913, lxi, 1803; ibid., 1914, lxii, 516; Johns Hopkins Hosp. Bull., 1914, xxv, 173-177.

Of the remaining 16 cases, 9 have not been heard from, 5 show recurrence or active manifestations, 1 is latent, and 1 is in good health. The average duration to date has been three years, exclusive of the one of twenty-five years' duration, the shortest one and the longest ten years. From present indications may of them will probably live a few years longer, but the prognosis of longevity in Hodgkin's disease is an uncertain factor even when there is an extensive involvement.

Since making these tabulations, Case 24, of twenty-five years' duration, shows remarkable change. The neck swelling has increased markedly, causing pressure on the larynx and trachea, and there is pronounced edema of the left arm and both legs. Fifteen years ago this patient received a Roentgen-ray burn, and on the advice of our roentgenologist, Dr. Leaming, this form of treatment is now contraindicated.

MICROSCOPIC PATHOLOGY. When one attempts to add anything to the microscopic pathology of Hodgkin's disease, little if anything will be new, for it has been very well covered by Reed, who made it what it is in this country. In the earliest description of this subject the original paper of Hodgkin, the gross appearance was completed by the term "cancer cerebriformis," unqualified but presumably because of the close resemblance to the gray matter of the central nervous system.

From the study of these cases it is my contention that the Dorothy Reed type is not a special form of Hodgkin's disease, but is the picture which makes Hodgkin's a distinct entity. Sections taken from various glands of a group enlargement give graded pictures from simple hyperplasia of lymphoid elements to the characteristic whirlwind fibrosis; but in some, if that group be the result of Hodgkin's disease, there will be that picture as described by Reed. It is a quantitative change, a stage not a qualitiative one. For this reason it is to be recommended that when one performs an operation in view of obtaining a gland for diagnosis, several glands should be excised as at either extreme a positive diagnosis is difficult. There is apparently no relation between the picture of glands and the clinical course of the disease. The so-called experimental Hodgkin's in the ape with its marked necrosis attributed by Bunting to the virulence of the infecting agent is something one rarely sees in human histology; but we occasionally see glands with marked endothelial hyperplasia and large areas of necrosis as the result of a pyogenic infection of low grade and of long duration. Over 125 sections taken from 23 cases have been carefully studied in this connection, and in only two specimens were areas of necrosis found. In these, two in each case, they were small, circumscribed foci of necrosis and polynuclear reaction.

To make different points clear, it is well to consider four stages which are by no means distinct but merge into one another imperceptibly in the same gland.

I. Hyperplasia of lymphoid elements.
II. Hyperplasia of endothelial elements with giant-cell formation.
III. Beginning fibrosis and loss of original architecture of gland.
IV. Fibrosis, atrophy of lymphoid elements, masking of characteristics.

The earliest pictures of Hodgkins disease are like those of any infection or irritation, a hyperplasia of lymphoid elements, and though the disease be suspected clinically, a histological diagnosis cannot be made, although "probably or suspected Hodgkin's" is justly resorted to. Sections from Cases 5, 6, 8, and 20 clearly demonstrated this point. In Case 5, with moderate enlargement of glands on the right side of the neck, many sections presented a hyperplastic lymphoid structure without other diagnostic features. This patient returned two years later with recurrence on the right side of the neck, and the glands were typically those of Hodgkin's with Reed cells, epithelioid cells, fibrosis, and eosinophiles. At the present writing this patient has a walnut-sized gland in femoral group and feels perfectly well.

From Case 6 another diagnosis of "suspected Hodgkin's disease" was made, and two years later the histology was unmistakable.

In Case 8 the examination of a small node offered nothing but hyperplastic lymphadenitis; the later examination of a larger gland gave a picture of moderately advanced healing. The histology of Case 20 had been particularly interesting. Several large areas of a nodular skin lesion had been excised and subjected to examination. All the earlier sections showed the same picture—fibroblastic reaction—fibrosis, round-cell infiltration, with a few eosinophiles and polynuclears and numerous small bloodvessels. Sections from glands gave a typical picture, and later sections from skin presented lymphogenetic areas with endothelioid cells and giant-cell reaction. This case demonstrates very well the primary compensatory lymphogenesis with subsequent involvement.

A point which appears to be of some value in this hyperplastic stage is the dearth or absence of the so-called germinal centres, for in glands of other sources they are of common occurrence. To conclude this stage it might be well to consider for a moment the derivation of the lymphocytes. The origin of lymphocytes under all conditions in health and disease is not known.

Fleming,[29] after demonstrating that efferent lymph was more cellular than afferent, in a classical article, basing his observations from glands of lower animals adopted the term "keimcentrum" to designate the peculiar and variable collection of cells seen in the follicles. This work was done on normal lymphatic tissue, and it was concluded that lymphocytes were produced by proliferation of mother cells of centres which in turn developed from certain cells of reticulum. Cases 8 and 19 seem to support this view, showing, as they do, lymphocytes developing in the centre of these centres in small follicular collections. These are the only instances of the kind that I have seen or heard of.

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[29] Arch. f. mikr. Anat., 1885, xxiv, 70.

That not all lymphocytes are developed from these germinal centres is supported by the following: (1) We occasionally see nuclear division in lymphocytes themselves; (2) they develop in certain regions of the body where there has never been any evidence of these centres, as in the omental fat, liver, lungs, and skin; (3) in certain glands definitely hyperplastic we fail to see germinal centres or their remains. Bearing on this point, Fleming believes that the "keimcentrum" is a transitory unit, increasing and decreasing,.appearing and disappearing at intervals. Yet, on the other hand, in some glands the seat of chronic inflammation we see their remains as hyaline fibrous pearls; and in Hodgkin's disease in the early stages when the lymphoid hyperplasia is at its height these centres are rarely seen. Yet these glands continue to enlarge, the predominating cell is lymphocytic, but they have no germinal centres to take origin from; (4) some writers believe they are derived from endothelium.

Pari passu with the increase in lymphoid structure appears a hyperplasia of endothelium and endothelioid cells. The endothelium of sinuses shows marked proliferation and scattered throughout the glands in variable numbers are cells of endothelioid type. These are most prominently seen in the reticulum of glands where many mitotic figures are made out. This picture is present in all the glands of series. With these smaller cells are seen many large ones more faintly staining with large polychromatic vesicular nuclei, containing one to three nucleoli; the so-called endothelioid, epithelioid, or giant mononuclear cell. These cells are present in eighteen of the specimens and multiply in part by karyokinesis and in part by direct division. Owing to the distribution of these cells they apparently develop from the reticulum. But when one reviews the literature on this subject he hesitates to say that they do develop in this manner for there are as many theories as there are writers. Ziegler believes they are formed for the most part from typical fibroblasts, swollen pathological forms. Longcope is of the opinion that they are derived from the reticulum.

A cell which has been prominent in this series and referred to by Symmers, perhaps ordinarily termed a giant mononuclear cell, is a large very faintly staining cell with lobed and partially divided pale nucleus. The protoplasm is not always clearly defined. We are beginning to place more weight on this cell, as it is quite as common as the Reed cell and seen many times when there is no evidence of the latter. We believe it to be a transition stage of the smaller endothelioid cells, these dividing by indirect division to produce like cells and by direct division the stage referred to to produce typical Reed cells. Transitions from the endothelioid cell to the Reed cell are clearly made out in the various sections. This is in contrast to Fabian, who believes they are formed from large lymphocytes, to Sternberg, Symmers, and Reed, who believe them formed from endothelium of sinuses, but conforms to the views of Longcope.

The Reed cells, giant multinuclear or sometimes termed mulberry cell, appear as a pathognomonic histological sign. At this date the description of such a cell is hardly necessary. In 17 of the 23 cases this cell has been found in varying numbers, containing from 2 to 10 nuclei of central and radial placement. In a few instances the nuclei have been of peripheral arrangement, simulating the architecture of the Langhans giant cell, but the morphology of the nucleus is distinctive.

Another cell type seen in one-quarter of the cases, which is very scarce and not of any value as an aid to the diagnosis, is a large clearly-defined cell with rather small deeply staining nucleus and large amount of eosinophilic protoplasm. They are seen occupying small spaces. The occurrence of eosinophiles in this disturbance was first noticed by Goldman,[30] who believed they were withdrawn from the blood by some specific chemotactic powers. This has been attributed by Bunting to the destruction of lymphocytes, polynuclears appearing in excess with the destruction of endothelium. Ziegler speaks of their presence being more common in the fibrosis. This conforms with Bunting's idea, and in reviewing the slides in this connection there seems to be this definite relation. They were present in large numbers in 50 per cent. of cases and absent entirely in six cases. Realizing that they rarely occur in large numbers in other conditions, and never in closely allied malignant states, their presence is of some significance by way of exclusion.

Plasma cells are commonly described as an important feature, but there seems to be a great diversity of opinion in the interpretation of the morphology of these cells. However, their presence or absence is of no diagnostic significance. In this study with the ordinary stains they were definitely made out in but a few instances.

The fibrosis manifests itself early in a thickening of the capsule and trabeculæ with a diffuse fibroblastic reaction and fine fibrillar fibrosis, the diffuse fibroblastic reaction being clearly made out at the onset of the endothelial reaction. As this process advances the preponderance appears to arise from trabeculæ, and in very late stages gives rise to a picture designated as whirlwind fibrosis. With the advent of fibrosis, lymphocytes become fewer and fewer, and though widely disseminated, there is in reality an atrophy.

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[30] Centralbl. f. Allg. Path., 1892, iii, 665.

The endotheliod cells in the same way give place to or in part give rise to the fibrosis. Bloodvessels become much thickened, and where there is a retention of germinal centres there is a central, intra- and perifibrosis. It is impossible to say whether the giant cells disappear entirely or give rise to the fibrosis. The glands lose their original follicular and characteristic pathological architecture, and the termination is a loss of the cellular fibrosis with hyalinization. This has been designated by Symmers[31] as "healing in Hodgkin's." The diagnosis cannot be made from such a gland or differentiated from the end-results of an acute lymphadenitis, tuberculosis, or syphilis. One, many, or all these gradations may be seen in one gland or its group.

In none of the cases has there been a clearly-defined picture of a transformed or superimposed malignancy. Case 23 was that of a middle-aged man, who had an axillary tumor of ten years' duration. At operation a massive axillary lymphatic involvement with direct extension into the pectoral muscles was found. The extension resembled in all respects the picture seen in the glands, lymphocytes with giant mononucleated and multinucleated cells and fibrosis. There is in this case, undoubtedly, one of the salient features of malignancy, but the histology remains typical of Hodgkin's disease.

VACCINES. In spite of the recent findings of an organism (isolated from glands, not Hodgkin's) similar to if not identical with the so-called B. hodgkini, several cases have been treated with vaccines.

Case 19 was operated on one year ago, and since this time has had energetic treatment (in the out-patient department) by a vaccine made from B. hodgkini obtained from the Museum of Natural History. He returned to the hospital a few weeks ago and several recurrent glands were excised. These were cultivated in the operating room under strictly aseptic conditions, on egg media, glycerin-phosphate-potato-agar, and the ordinary media, and all tubes were sterile at the end of one month.

Case 17 has been treated with vaccines and Roentgen-ray for one year. Although she feels in better health the glands are larger and the breast is infiltrated.[32]

Cases 16 and 24 have progressed with constantly increasing and long-continued dosage. They have had a fair trial, but since this organism is not the specific cause it seems futile and a waste of time and material to continue.

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[31] New York Med. Jour., May 20, 1911.

[32] Under Roentgen-ray treatment alone all glands have reduced greatly in size, and the breast has returned to normal.

SUMMARY OF BLOOD FINDINGS. For this summary only those blood examinations which have been studied and later reviewed by Dr. Warren are considered. Several examinations were made on 10 of the cases, and the average is found to be as follows:

No.	Hb.	Red blood cells.	White blood cells.	Poly-morpho-nuclears.	Lym-pho-cytes.	Large mono-nuclears.	Transi-tionals.	Eosino-ophiles.	Baso-philes.
4	70	4,150,000	74,000	91.7	3.3	2.3	2.4	.0	.3
6	60	4,300,000	15,000	76.8	6.7	0.8	12.6	2.3	0.5
11	75	5,600,000	20,000	80.0	11.0	1.8	6.0	0.5	1.15
15	58	3,500,000	14,000	69	20	2.3	7.3	1	0.3
16	68	4,360,000	12,000	68	22.3	2.3	5.0	2.3	0
17	80	3,750,000	11,000	78	11.5	3.3	5.8	0.6	0
18	90	5,550,000	19,000	72.5	19.6	0.6	5.3	1.3	
19	94	4,800,000	16,000	73.5	17	0.5	7.0	0.6	
20	56	4,700,000	62,000	92.0	1.5	2.3	3.5	1.3	0.15
24	68	4,000,000	12,000	71.0	15	5.3	6.3	1.5	0.6

With some of the other cases the hemoglobin has varied between 40 and 110 Sahli corrected and the red cells from 2,944,000 to normal. These two units vary directly with the course and severity of the disease, and are of no diagnostic importance.

The total leukocytic count and differential is a very variable factor. It does not seem to bear any direct relation to the duration of the process. Considering the microscopic pathology we fail to find evidence of acute inflammatory reaction (necrosis or polynuclear infiltration) in these cases with high leukocytosis. It is, however, dependent on the severity or toxicity of the case and remains high in this type of case when the temperature drops to normal. This leaves us to account for it for the greater part on the extent of involvement of the lymphatics and internal organs. Very good examples are offered in Cases 4 and 20, the former reaching 104,000 the latter 112,000. Both these cases presented an extensive general involvement. A leukopenia was observed in only one case (Case 10).

In the differential counts the polynuclears are relatively and absolutely increased, the lowest being 53 per cent. and the highest 97 per cent. Blood platelets are increased.

As seen in the table of blood findings the transitionals are found to be variable, though in general increased, in seven of these being over 5 per cent., the highest being 12.6 per cent., the average 6.6 per cent. The series is too small to lay too much stress on the diagnostic importance of a high transitional count, which is considered by Bunting to be diagnostic when accompanied by chronic lymphatic enlargement. We have recently had a case of primary large round-cell sarcoma of the mediastinum with extension to clavicular glands which gave a transitional differential of 13.3 per cent. A mistaken diagnosis from blood findings alone could easily have been made in this case. For years a relative lymphocytosis had been considered the usual finding, but none of the late reports show this. In over 33 counts the average was 14 per cent., and 30 to 40 per cent. is unusual. The conclusions from such a small series are not of much value, for the picture is quite a variable one. The quotation of Fabian[33] in this particular seems quite appropriate: "The blood picture changes in one-fifth part of an observation."

No.	Case.	Adm. No.	Case index.	Path. No.	Result.
1	L. M.	. . .	May 24, 1909	286	Lost trace.
2	P. B.	B–1	July 18, 1909	588	Lost trace.
3	F. DeM.	B–181	Feb. 17, 1910	1910	Lost trace.
4	S. J.	B–257	Dec. 24, 1910	2056	Died.
5	H. S.	A–742	Aug. 18, 1910	3530	Living; recurrence.
6	M. D.	A–1439 D–3656 7736 5568	. . . .	5503 8938	Died.
7	M. Gr.	D–1554	Feb. 11, 1911	. . . . . .	Lost trace.
8	J. C.	A–1819	July 19, 1911	6897	Died.
9	A. H.	D–1893	July 17, 1911	6572	Lost trace.
10	F. K.	B–2000	Oct. 10, 1911	7653	Died.
11	A. V.	H–2218	Dec. 25, 1911	8300	Lost trace.
12	Mr. F. P. P.	2888	Aug. 5, 1912	B–323	In good health.
13	G. S.	D–3998	. . . .	. . . . . .	Died (?)
14	G. S.	D–3998	Aug. 9, 1912	B–355	Died (?)
15	C. S.	A–4862	May 7, 1912	B–3183	Died.
16	W. B.	B–4380	Oct. 4, 1912	B–4529	Recurrence.
17	E. L.	A–5070	April 30, 1914	B–6581	Active.
18	P. B.	A–6036	May 18, 1914	B–6780	Lost trace.
19	A. B.	A–4987	May 19, 1914	B–6838	Active.
20	M. G.	A 2245	Sept. 28, 1911	7608 7675 7814 8744	Died.
21	P. Q.	B–6071	Mar. 4, 1914	B–7045	Died.
22	M. S.	D–6192	June 5, 1914	B–7028	Living (metaplasia).
23	D. C.		May 5, 1912	B–9606	Dead (?)
24	O. G.	A–5472	Dec. 1, 1914	B–8762	Active.

CONCLUSIONS. 1. Dorothy Reed Hodgkin's is not a type but the classical picture; it stands as a distinct entity.

2. The prognosis of Hodgkin's disease is difficult. It is impossible to say that a case is cured.

3. The treatment is excision of all foci of infection and Roentgen-rays.

4. Vaccines are of no value.

5. For diagnosis in lymphatic disturbances more than one gland should be obtained.

6. The following evidence is given to support it as an infection, bacterial or protozoan in origin: (*a*) the histology is that of an inflammatory reaction; (*b*) injections of gland emulsions have caused temporary lymphatic enlargement in lower animals (literature);

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[33] Centralbl. f. Allg. Path., 1911, xxii, 145.

(*c*) the fever resembles closely that of other infections; (*d*) the leukocytosis; (*e*) the exudate when serous surfaces are involved.

7. The specific organism has not been isolated. A detailed report will appear later to support this.

In concluding, I wish to thank Dr. Warren and Dr. Mann who have made this work possibly by their stastistics and coöperation, and Dr. McCreery for his earlier work on the histories.

THE CITRATE METHOD OF BLOOD TRANSFUSION IN CHILDREN.

By Richard Lewisohn, M.D.,
NEW YORK CITY.

The citrate method of blood transfusion which I described in January, 1915,[1] has rapidly gained great popularity. Theoretical objections against the mixture of blood with an anticoagulating substance have been overcome by practical experience. This has proved that the citrated blood is clinically as effectual as pure blood. The great simplicity of the method, which makes blood transfusion technically as easy as an ordinary saline infusion, has, of course, widened the applicability of the former, even in smaller communities, and will certainly serve to popularize blood transfusion.

The effectiveness of citrate of soda as an anticoagulant is, of course, nothing new. In fact, we all know that for many years it has been used quite extensively in the laboratories for the purpose of preventing blood from clotting. The dose used for this purpose was 1 per cent.

I have often wondered why so much time has been spent in devising technically most complicated methods (vessel anastomosis, syringes, etc.) instead of applying this well-known drug in human blood transfusion.

The answer is given in the experimental part of my work, which I published in detail a few months ago.[2] These experiments brought to light two important facts;

1. That it is unnecessary to use 1 per cent. sodium citrate to prevent coagulation of the blood, but that 0.2 per cent. suffices.

2. That sodium citrate used at the ratio of 1 per cent. would prove fatal in large transfusions of blood (1000 c.c.).

This last fact answers the question why sodium citrate has not been applied before in human blood transfusion. The fear that this anti-coagulant might prove to be toxic when used in large doses is a well-founded one. That sodium citrate may be safely applied for intravenous injection of large quantities of blood, without risk or danger to the patient is based on the fact that my experiments showed that a mixture of 0.2 per cent. citrate of soda is sufficient to prevent coagulation.

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[1] Med. Rec., New York, 1915, lxxxvii, 141.

[2] Surg., Gynec. and Obstet., 1915, xxi.

These results of my animal experiments were of special importance on account of another publication on this subject which appeared contemporaneously with mine. Weil[3] reported that he had injected up to 350 c.c. of blood mixed with 3.5 grams of sodium citrate. He had used this large dose of citrate because, evidently through some error in his experiments, he had come to the conclusion that 1 per cent. sodium citrate (*i. e.*, the dose used in laboratory work) was necessary to prevent coagulation. There was no warning in his paper against the possible toxicity of sodium citrate at the 1 per cent. ratio. My animal experiments show conclusively that if anybody had applied Weil's dose for a large transfusion on the human being the results would have been fatal. The citrate method, which has proved harmless and efficient, when applied at the 0.2 per cent. ratio, would surely have been abandoned after a few trials if my experiments had not pointed out the toxicity of Weil's dose and thus prevented others from using citrate at the ratio of 1 per cent.

The atoxicity of sodium citrate at the 0.2 per cent. ratio (*i. e.*, 2 grams of sodium citrate to 1000 c.c. of blood) is best proved by the use of this method for transfusion of blood in small children. Blood transfusion in infants has great possibilities. Melena neonatorum, primary and secondary anemias, typhoid hemorrhages, some cases of marasmus, etc., yield remarkably well to blood transfusions and often show most startling results. All the older methods presented the greatest technical difficulties when applied in these little infants, and therefore blood transfusion has not been used sufficiently in small children.

The technic is exactly the same as described for adults.[4] The donor's vein can be punctured proximally or distally, the direction to be chosen according to the individual case, whichever way the blood runs with the greatest facility into the glass receptacle. The blood is mixed in the glass jar with a 2 per cent. sterile solution of sodium citrate at the ratio of 1 to 10 (*i. e.*, 10 parts of solution to 100 c.c. of blood). For the reintroduction of the blood a very fine needle or cannula can be chosen. Thus one can inject the blood even in small children through a superficial arm vein of the finest caliber. This obviates any extensive dissection. By using so fine a needle one assures the slow injection of the blood and prevents the danger of sudden overloading of the circulatory system. The salvarsan flask is attached to a stand and the blood allowed to run into the vein drop by drop (in 1 case the injection of 350 c.c. thus took nearly an hour, and the three-year-old child stood this rather large quantity of blood very well, just on account of the slow injection).

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[3] Jour. Amer. Med. Assn., 1915, lxiv, 425; Clin. Conf., Mt. Sinai Hosp., Jan., 1915.

[4] Loc. cit.

Among the 30 cases of blood transfusion in which I used the citrate method 7 were children.

The first child in whom the new method was applied was a boy, aged five years, with extensive burns. He received two transfusions of 150 c.c. of blood. His hemoglobin was raised from 42 to 72 per cent. The improvement in the general condition of the child was most remarkable.

The second case was a child, aged three years, with hemorrhages from the intestinal tract. This child received its first transfusion (Lindeman's method) in August, 1914. The hemorrhages then stopped for six months. The patient was readmitted to the hospital in February, 1915, on account of the recurrence of hemorrhages. A second transfusion of 200 c.c. of blood (citrate method) from the father of the child failed to stop the hemorrhages. An exploratory laparotomy was then decided upon, preceded by another transfusion of 450 c.c. of citrated blood. An exploration of the stomach and duodenum was negative. Two weeks later the hemorrhages began again, and since the child was very anemic, another transfusion was advised; this time the Unger method was used. The improvement following this transfusion was only temporary and a fifth transfusion (citrate method) was given in May, 1915. Since then the child has picked up wonderfully. The hemorrhages have stopped entirely. The child appears to be in perfect health; but palpation of the abdomen now reveals an enlarged spleen. This probably explains the hemorrhages from the stomach. This case shows how much can be accomplished by repeated blood transfusions. In regard to the new method it shows that citrated blood is as efficient as unmixed blood. The reason that the clinical result of the last transfusion was so much better than that of the three previous transfusions (two done with the citrate method and one with the Unger method), is probably based on the fact that the blood of the last donor was exceptionally well adapted for this child's blood. We know very little about the relative values of the blood of different donors. But it certainly is advisable, in cases where one transfusion failed to give good results, to try another donor.

The third case was a child, aged six months, suffering from an aplastic anemia. The child received two transfusions, each of 100 c.c. The baby had remarkably improved and showed an excellent color. The child was readmitted two weeks later on account of severe gastro-enteritis, to which it succumbed on August 15, 1915. In little infants a small amount of blood ought to be introduced repeatedly in order to safeguard against sudden overloading of the circulatory system.

The fourth case was a nine-months-old baby; the indication for transfusion was a severe anemia. The child received 100 c.c. of blood and the hemoglobin was raised from 16 to 26 per cent. The child's condition was decidedly improved. This was the only case in this series which had quite a severe reaction (rise of temperature to 102° F. without chill) following the transfusion.

The fifth case seems to me to be the most interesting in this series. A seven-year-old girl had profuse intestinal hemorrhages on the fourteenth day of typhoid fever. The hemorrhages were so profuse that the child was in a dying condition; she was unconscious and the radial pulse was not palpable. An immediate transfusion was done; the blood was taken from the mother; 400 c.c. of blood were transfused. The change in the condition of the child was most remarkable. She reacted while she was receiving the blood and the pulse reappeared. The hemorrhages stopped and no further bleeding occurred during the course of the illness. The disease ran a very severe course, and to combat the marked sepsis a second transfusion was deemed advisable. This was again done by the citrate method, three weeks after the first transfusion. The symptoms of severe typhosepsis were not changed by this transfusion and the child died seven weeks after the onset of her illness. It is interesting to note that this child had a very marked anaphylactic reaction after the first transfusion, though the blood was taken from the mother. No reaction occurred after the second transfusion, for which a professional had been selected and properly tested. This case tends to show that theoretical objections against citrated blood are not based on facts; on the contrary, the citrate transfusion ought to be the method of choice in hemorrhages, because the coagulation time of the recipient's blood is shortened immediately after the introduction of citrated blood.

The sixth case was a three-year-old boy, a hemophiliac, who was very much exansanguinated from a severe hemorrhage (bite o the tongue) which had lasted for twenty-four hours. He received 250 c.c. of citrated blood and the bleeding stopped immediately; his hemoglobin was raised from 19 to 39 per cent.

The last case, the youngest in this series, was a baby, aged twenty days, which had been bleeding since its birth from the umbilicus; 80 c.c. of citrated blood stopped the hemorrhages immediately and permanently; the baby was taken home a few days later.

REVIEWS

Modern Aspects of the Circulation in Health and Disease. By Carl J. Wiggers, M.D., Assistant Professor of Physiology in Cornell University Medical College. Pp. 361; 104 illustrations. Philadelphia and New York: Lea & Febiger, 1915.

The ever-increasing knowledge of the physiology and the pathological physiology of the circulation, through the studies of both the physiologist and clinician, makes necessary a book or a monograph on the subject available to those who are unable to follow the large amount of literature upon the subject. To supply this need, Dr. Wiggers, long a student of the circulation, has brought out the present work. The monograph is divided into three parts: part one deals with the present-day conception of the maintenance of the circulation in health; part two describes the graphic methods of studying the circulation for the clinician; and part three correlates the first two parts with the simpler methods of diagnosis available at the bedside. With the subject matter arranged in this manner, one is enabled to follow readily the application of the physics of the circulation to pathological processes, so that the information derived thereby is of use in the study of clinical material. This book is not written solely for the man who wishes to be thought up to the minute, but is in truth for the man who wishes to know and to study a clear and thorough exposition of the modern concept of the cardiovascular system which has revolutionized this branch of medicine in the past ten years. One learns the rationale of the uses and the interpretation of the results from the use of the sphygmomanometer, the electrocardiograph, the phonocardiograph, the polygraph, and other instruments of precision employed in the study of the circulation. The aid that the work is bound to give those interested in clinical medicine will insure for it a marked success and a particularly hearty reception from those who wish to know exactly the whys and wherefores of the various procedures in the study of the circulation. J. H. M., Jr.

Soziale Pathologie. Von Prof. Dr. med. Alfred Grotjahn, Berlin. Second edition. Pp. 532. Berlin: Verlag von August Hirschwald, 1915.

The second edition of this work comes enriched by three years' experience the author has enjoyed while in charge of the Section on Social Hygiene in the Hygienic Institute of the University of Berlin. While he has set himself a very ambitious task both as to size and complexity, he has performed it in a most interesting fashion, has furnished a great deal of valuable material, and, through the manner in which he has utilized this material to mould broad general concepts in regard to the relation between disease and social questions, has definitely supported his claim to originality.

The work contains two main divisions, a special and a general part. The first deals with a vast number of individual diseases, such as individual acute and chronic infections, circulatory diseases, respiratory diseases, sexual diseases, nervous and mental diseases, occupational diseases, diseases particularly affecting women, infants and children, surgical diseases, ocular diseases, and others. Each disease in turn receives a systematic investigation to determine social-pathological data, such as the frequency of the particular disease, the amount of disability and loss of income it occasions, the prevalence of slight and abortive forms of the disease, the broad etiology of the disease, entailing a consideration of habits nutrition, environment at home and at work, etc., the effect of the disease on social conditions, medical treatment, insurance, and, particularly, the social treatment and prevention of the disease.

This first part giving individual consideration to each special disease prepares the way for the second part dealing with problems of wider range. The relative importance from a social stand-point of different groups of diseases, and especially the great influence of the diseases of infants, children and women, the relation of the physician to social medicine, the relation of social status to disease, the results of disease, for example, in shortening life and in limiting income, are discussed. The value of segregation in the case of many diseases is emphasized. Problems associated with degeneracy and eugenics receive very special consideration. The author is particularly interested in the subject of the prevention of conception, first, as a preventive of the transmission of diseases or diseased tendencies, second, as a means in certain cases to obtain fewer and more vigorous offspring, and, third, as a real danger, if it is abused to the extent of unduly reducing the birthrate. A steadily falling birth-rate he considers far more destructive for the German race than even the war now raging between the Germans and the English. However, a falling birth-rate that may be detrimental to a nation as a whole at our present stage of uncivilization, is not demonstrated by the author to be necessarily injurious to the individual himself, except as a part of that nation.

It would be impossible to summarize the author's views or discuss his conclusions in a brief review. Many of the questions presented are, and will long remain, unsettled. In regard to many of the subjects in which science has clearly shown the path to follow, the difficult task still remains to see that the proper measures are carried out.

C. M. M.

THE CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Vol. IV, No. 3, June, 1915. Pp. 196; 90 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THE most important feature of this number of *Murphy's Clinics* is "A Clinical Talk on the Diagnosis of Injuries of the Carpus," a subject which fully justifies the addition of fifty-eight pages to the current literature. The more common injuries and their diagnostic signs are admirably presented from the stand-point of anatomic reasoning and are well illustrated by drawings and roentgenograms. The clinical aspects of four selected cases emphasize the possibility of accurate diagnosis and the necessity for appropriate treatment in a class of fractures and dislocations not infrequently neglected. In "A Talk on Appendicitis," Dr. Murphy makes the astounding statement that "the average hospital mortality rate is just a little over 10 per cent." The statistics are taken from the printed annual reports of hospitals, and include appendicitis cases of all classes. Dr. William J. Mayo gives a talk on "Unsuccessful Gastro-enterostomy for Ulcer: An Analysis of its Causes, Suggestions for Better Technic." His final statement, "Looked upon as a whole, I think nothing in the field of surgery has given such good results as the operative treatment of ulcer of the stomach and duodenum," suggests the thought that many surgeons will have to gain an experience with the more modern principles and master the best technic before they can share this optimism.

In the nine cases of various types with Dr. Murphy's comments and the descriptions of operations, the reader will find new ideas, and perhaps old ideas presented in a new way, in sufficient number to commend this number of the *Clinics*. G. M. L.

THE CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Vol. IV, No. 4, August, 1915. Edited by DR. P. G. SKILLERN, JR., of Philadelphia. Philadelphia and London: W. B. Saunders Company, 1915.

THE August number of *Murphy's Clinics* is edited by Dr. P. G. Skillern, Jr., of Philadelphia, and gives a summary of each case. There are thirty-two headings, an unusually large proportion of which deal with the surgery of the nervous system and are discussed by Dr. Mix. The summary will be found useful to the regular subscriber who cannot spare the time to read what had already been covered in previous numbers and the frequent references will enable the new reader readily to find the collateral subjects in former volumes.

The reviewer cannot feel convinced that treatment of the primary lesion of syphilis with sodium cacodylate masters the syphilis problem. In the case of papilloma of the bladder it is noted that the three glass test is dwelt upon as a method of determining the source of hematuria and that mention of cystoscopy is not made. In the case of "Typhoid Spondylitis in a Typhoid Carrier," drainage of a macroscopically normal gall-bladder and removal of a symptomless appendix furnish a striking illustration of how arthritis cases are handled. There are so few roentgenograms of typhoid spine on record that it is to be regretted that there is no mention of Roentgen-ray examination in this case. G. M. L.

APPLIED IMMUNOLOGY. THE PRACTICAL APPLICATION OF SERA AND BACTERINS PROPHYLACTICALLY, DIAGNOSTICALLY, AND THERAPEUTICALLY, WITH AN APPENDIX ON SERUM TREATMENT OF HEMORRHAGE, ORGANOTHERAPY, AND CHEMOTHERAPY. By B. A. THOMAS, A.M., M.D., Professor of Genito-urinary Surgery in the Polyclinic Hospital and College for Graduates in Medicine; Instructor in Surgery in the University of Pennsylvania; Associate in the William Pepper Laboratory of Clinical Medicine, and R. H. IVY, M.D., D.D.S., Assistant Instructor in Surgery in the University of Pennsylvania; Instructor in Genito-urinary Surgery in the Polyclinic Hospital and College for Graduates in Medicine, Philadelphia. Pp. 359; 5 colored inserts and 68 illustrations. Philadelphia and London: J. B. Lippincott Company, 1915.

UNLIKE the farmer's basket of apples, this excellent book presents its faults in the opening chapters and thereafter improves steadily in worth and lucidity to the end. At the worst the faults are not important and consist of a certain carelessness in writing, especially in the introduction, and at times of a lack of that proper distribution of emphasis which is so helpful to the uninitiated. Thus isocytolysins are mentioned impartially with toxins and agglutinins, and such subjects as the antityphoid extract of Jez, anticarcinomatous extracts, and the use of crotalin in epilepsy are enumerated merely to be condemned. Apparently the isolation of the rabies organism takes place between the twelfth and the sixty-fourth pages.

Unhesitatingly, however, it may be stated that the book succeeds most admirably in its object "to crystallize and detail the practical phases of serum and bacterin application in medicine, thereby enabling the student and general practitioner, with even a slight laboratory experience, to appreciate the significance of, and more competently apply the principles underlying, immunology." No more satisfactory brief description of the Widal phenomenon, the Wassermann test, tuberculin tests and tuberculin therapy has been published. The opsonic index and bacterial inoculations receive attention disproportionate perhaps to the other chapters, but certainly not to the importance of these topics. Finally, the appendices, especially that on chemotherapy and the various necessary technics, add still further to the usefulness and value of this very satisfactory work. O. H. P. P.

Radiography, X-ray Therapeutics, and Radium Therapy. By Robert Knox, M.D. (Edin.), M.R.C.S. (Eng.), L.R.C.P. (Lond.), Hon. Radiographer, King's College Hospital, London; Director, Electrical and Radiotherapeutic Department, Cancer Hospital, London, etc. Pp. 406; 64 plates, 246 illustrations, and frontispiece in color. New York: The Macmillan Company, 1915.

The author of this admirable book is, by way of introduction, a well-known English roentgenologist whose talent is recognized on both continents. His connections with numerous hospitals and in the capacity of editor of the *Archives of the Roentgen Ray*, having recently succeeded Dr. Deane Butcher, are additional indications of his high standing among roentgenologists of his own country. The English language is lamentably weak in books on roentgenology, which are of use to those specializing in this branch or that can be safely recommended to those beginning a study of the subject, but this is one of the very best so far published in this language. It is concise and at the same time comprehensive, and with a very few exceptions is thoroughly up-to-date, embodying the most modern views and methods and showing conversance with the latest literature. It is a book that can be of service to the roentgenologist and radium therapeutist, and is one of the very few that may be recommended to the student with a view of supplying him with useful knowledge without fear that he may be misinformed or misled. A section of reasonable length is devoted to the description and use of different forms of Roentgen-ray apparatus and tubes, with, quite naturally perhaps, a decided leaning toward those of foreign design. One chapter deals with modern methods of localization of foreign bodies, which has become a most important use for Roentgen-ray work abroad during the past year. A very useful and instructive section is devoted to a roentgenologic study of normal bones and joints and of bone development. In his presentation of gastro-intestinal diagnosis the author is extremely conservative, and possibly too much so, although he can hardly be criticised for this in view of the rapid strides being made in this department of roentgenology and the numerous and radical changes constantly being made in technic. The diagnosis of conditions of the thoracic viscera and urinary tract is far above any criticism. The entire diagnostic section is profusely illustrated by an excellent selection of reproductions, for the appearance of which the publishers deserve the greatest praise. About one-third of the book is devoted to roentgen and radium therapeutics. The author's description of roentgen technic is concise but thorough, and the freedom of the text from case reports is commendable. The section on radium therapy is preceded by a chapter on physics of radium, by Mr. C. E. S. Phillips. In conclusion, this book can be conscientiously recommended to roentgenologists for reference, to physicians and surgeons as a means of increasing their knowledge of the subjects discussed, and to the student in roentgenology as a text-book. H. K. P.

A LABORATORY MANUAL AND TEXT-BOOK OF EMBRYOLOGY. By CHARLES WILLIAM PRENTISS, A.M., PH.D., late Professor of Microscopic Anatomy in the Northwestern Medical School, Chicago. Pp. 400; 369 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

"THIS book represents an attempt to combine brief description of the vertebrate embryos which are studied in the laboratory, with an account of human embryology adapted especially to the medical student." With these words, the author began his preface, and when one examines the worthy result of his efforts one is doubly regretful at the loss which American science, as well as his personal circle, has sustained in the author's death, shortly after the completion of this volume. In the introduction he urges the value of all well-preserved human embryos to the investigator, and suggests that aborted embryos and those obtained by operation in case of either normal or ectopic pregnancies should always be saved and preserved by immersing them intact in 10 per cent. formalin or Zenker's fluid. One might add that the history of the patient should be as complete as possible on all points pertaining to the age of the embryo. In Chapter I, in the description of germ cells and fertilization, reference is made to the substance, which F. R. Lillie has shown to be produced in the ova of the sea-urchin, and named by him fertilizin. This substance, Lillie regards as an amboceptor essential to fertilization, with one side-chain which agglutinates and attracts the spermatozoa and with another side-chain which activates the cytoplasm and initiates the segmentation of the ovum. After describing the segmentation of the fertilized ovum in the several vertebrate classes (Chapter II), the study of chick embryos is briefly outlined in Chapter III. The stages selected are of twenty-five, thirty-six, and fifty hours' incubation periods, which are sufficient to show important stages in the development of the main systems, of body form, and of the membranes. Chapter IV is devoted to fetal membranes and early human embryos. Illustrations are given of several of the young embryos which have been carefully studied during the last few years, and the anatomy of a 4.2 mm. human embryo, studied and described by His, is given in some detail. Illustrations of twenty-five stages, up to the end of the second month, are shown. As to the method of estimating the age of young embryos, the author judges it more correct to compute the age from the end of the last menstruation, or even, according to Grosser, from the tenth or twelfth day before the first missed menstrual period. In Chapters V and VI the anatomy of pig embryos of especially 6, 10, 18 and 35 mm. length is described by the aid of dissection and serial sections. The author was well-known for his ability in dissecting these delicate objects, and has given a brief description of his method. The dissecting instruments include a binocular dissecting microscope and a sharp safety-razor blade, and the embryo must be hardened carefully to have the right consistency, neither too brittle nor too soft. In the remaining six chapters are given descriptions of the development of the various systems and organs of the human body. Frequent reference is made to recent work, and the numerous illustrations are drawn, for the most part, from the works of the main contributors to the science. Many of the descriptions are necessarily brief, but the text is always clear, and the book, as a whole, will surely realize its author's aim in usefulness to the student. W. H. F. A.

MEDICAL APPLIED ANATOMY. By J. B. JOHNSTON, M.B., CH.B., Lecturer on Anatomy, University College, London; lately Lecturer on Medical Applied Anatomy, Edinburgh Post-Graduate Courses in Medicine and Surgery. Pp. 436; 146 illustrations, and 3 full-page plates in color. London: A. & C. Black, Limited, 1915.

THE author of this work has endeavored to show the applications of anatomy to the study of clinical medicine, and while there are certain anatomical sections of the book which even by the widest stretch of the imagination, can have no possible direct relationship to internal medicine, still on the whole his efforts may be said to be highly successful. In order to properly carry out his purpose the subject is treated according to systems rather than according to regions as is done with surgical applied anatomy. The first system discussed is the central nervous system and it comprises nearly half the book. Then follow chapters upon the organs of special sense, the digestion, the vascular, the respiratory and genito-urinary systems and the ductless glands. The anatomy of the various parts is described and with the anatomical description there is given a careful explanation of how this applies to physical diagnosis, what relation it has to the physiology of the part, how pathological changes effect the normal anatomy and physiology, how therapeusis changes normal or abnormal conditions and a multiplicity of other facts an explanation of which is extremely hard to find in ordinary text-books.

The book is intensely interesting and extremely practical. It is distinctly a border-line book which will fulfil a very definite purpose in linking more closely the science of anatomy with the art of internal medicine. J. H. M., Jr.

Lead Poisoning. By Sir Thomas Oliver, M.A., M.D., M.R.C.P., Consulting Physician, Royal Victoria Infirmary, and Professor of the Principles and Practice of Medicine, University of Durham College of Medicine, etc. Pp. 294. New York: Paul B. Hoeber.

This book is made up of a series of lectures delivered by the author in the Royal Institute of Public Health, Russell Square, London. He treats the subject of lead from the social and industrial points of view as well as from the medical, and does it all in such a simple and clear-cut way as to be entirely intelligible to both the laity and the profession. In the first portion of the book there are placed before the reader the various and sundry ways by which lead may gain entrance into the body; the details of the smelting, the manufacture of red and white lead, the dangers of the lead paints, of printing and type-founding, etc., all being covered. This is followed by a presentation of the symptomatology of lead poisoning, and finally in the last few chapters he discusses its treatment from both the preventive and curative points of view. As a curative agency he is quite enthusiastic about the electrolytic treatment, with which he seems to have experimented considerably. In an appendix of sixty pages he embodies the English factory and workshop orders relating to lead poisoning.

Oliver's experience with this metal, the most widely used metal but iron, has apparently embraced its every aspect, and he speaks largely out of this experience, at the same time presenting many statistics, tables, and opinions from other investigators.

T. G. M.

Edema and Nephritis. By Martin H. Fischer, M.D., Eichberg Professor of Physiology in the University of Cincinnati. Second edition; pp. 695; 160 illustrations. New York: John Wiley and Sons, 1915.

This work is a combination of the author's two previous works upon *Edema* and *Nephritis* respectively, with certain additions particularly concerning the application of the colloid chemical theory to such fundamental physiological phenomena as absorption and secretion, hemolysis and muscular contraction. In calling attention to colloid reactions and to the probability that these reactions play an important part in many fundamental physiological phenomena, the book is of considerable interest and value, and will repay reading. It is unfortunate, however, that the author so frequently insists, quite without adequate proof, that these colloid reactions can be the whole explanation of these physiological and pathological phenomena. This practice renders the work to a dangerous degree misleading.

In discussing the treatment of nephritis with anuria or oliguria the author still recommends the injection of an alkaline hypertonic sodium chloride solution, a therapy against which exists the weight of repeated careful studies by many investigators upon the affects of sodium chloride in nephritis. Clinical and experimental studies emphasize the positive danger of chloride administration in many types of nephritis, especially in those associated with diminished output of urine and with edema. Indeed, this therapy is an illustration of the unfortunate errors that might spring from an unqualified acceptance of the theory advanced by the author.

J. H. A.

The Operative Treatment of Chronic Intestinal Stasis. By Sir W. Arbuthnot Lane, Bart., M.S., F.R.C.S., Senior Surgeon to Guy's Hospital and Emeritus Surgeon to the Hospital for Sick Children, Great Ormond Street. Third edition. London: James Nesbit & Co., Limited. Chicago: Medical Book Co., 1915.

The first chapter of this book contains the author's well-known views concerning the evolutionary development of the mechanism producing chronic intestinal stasis. He opens his discussion by noting the changes in the skeleton arising from strain and then proceeds to demonstrate that comparable alterations are found in the gastro-intestinal tract from like cause. The reader will be interested in the author's description of the ills that result from intestinal stasis as well as the remarkable changes that are noted after the colon has been removed. Although excellent results were reported in earlier papers following lateral and end-to-side anastomosis the author has discarded these in favor of colectomy and end-to-end anastomosis. The technic of operation is fully described. It is to be regretted that in the last monograph, which stands as a *résumé* of his work, the author has failed to include a summary of the end results in all cases thus treated. The second and third chapters are written by Jordan and Mutch, and deal with the investigation of chronic intestinal stasis by the Roentgen-rays and the bacteriochemistry of the small intestine. A few pages are given to quotations from Mackenzie's *Diseases of the Heart,* showing that what he once termed "X-disease" is identical with chronic intestinal stasis. The final chapters contain two papers which the author published nearly thirty years ago and deal with skeletal changes incident to occupation. F. E. K.

THE HEART IN EARLY LIFE. By G. A. SUTHERLAND, M.D., F.R.C.P., Senior Physician to the Hampstead and North-West London Hospital; Physician to Paddington Green Children's Hospital. Oxford University Press.

SUTHERLAND has written a very readable book. As he himself says, he is clearly a disciple of Mackenzie and shares the latter's well-known optimism. As an illustration of this, one-quarter of the book is given up to functional disturbances of the heart, in which he goes into not only the question of functional arrhythmia but of functional dilatation, functional murmurs, and the subjective phenomena of cardiac disease, which very frequently depend on functional disturbances only. It seems well to dwell upon this subject at length, for no doubt not only the laity but many physicians have taken all murmurs and all irregularities too seriously. As to whether the placing of paroxysmal tachycardia in a section by itself designated "The Borderland between Functional Disturbance and Organic Disease of the Heart" is wise, may be questionable. Personally, the dogmatic separation of paroxysmal tachycardia and auricular flutter is at least clinically a useful division, but there are many who maintain that this division is quite unnecessary. However, Sutherland's division tends to emphasize the fact that in the majority of cases of paroxysmal tachycardia we are unable to point to a satisfactory cause. Here, perhaps, it is the limitation of our method of the minute study of the cardiac muscle and not the lesion that is lacking. The study of a few cases carefully and from many angles may be very instructive. Apparently this book has been written from such a stand-point. Though one misses the deductions drawn from a clinical experience which furnishes large groups of cases of a peculiar lesion or pathological activity, yet the material used is used well. C. A. F.

EVOLUTION AND DISEASE. By J. T. C. NASH, Captain, R.A.M.C., T.F., S.S., Diplomate in Public Health, University of Cambridge; Doctor of Medicine, University of Edinburgh, etc. Pp. 73. New York: William Wood & Co., 1915.

JUST as evolution has wrought changes in man's physical being so has evolution brought about variations in the diseases of man. The trend of the author's thought upon this matter is indicated in the following quotation from his chapter upon the evolution of disease germs: "I am not one of those who believe that disease germs entered one by one into the ark to transmit each its own species unchanged through the ages. It is very questionable if at that early stage of human history any pathogenic organisms existed, though probably their prototypes in the form of harmless saprophytes were to be found. As men began to crowd together . . . so gradually came into existence the necessary factors which resulted . . . in the evolutionized forms of organisms which are accountable for disease." With this idea in mind Nash has reviewed historically the epidemics of the middle ages. Following this he has dealt with some of the present-day scientific evidences of evolution in relation to disease. This contribution to the subject of evolution, while briefly stated, is broad in outlook, thought-producing, and gives one a larger and truer conception of disease.

T. G. M.

SIMPLIFIED INFANT-FEEDING. By ROGER H. DENNETT, B.S., M.D., New York Post-Graduate Medical School, etc. Pp. 355; 14 illustrations. Philadelphia: J. B. Lippincott Company, 1915.

THE author presents infant-feeding purely from the clinical standpoint, and by outlining but one method of procedure reduces the subject to the simplest possible terms. This will doubtless assist the beginning student to get a clear view of the fundamentals, but the general practitioner will regret the strict limitations of this book. Theories and generalities are almost entirely disregarded here and the directions given are explicit and specific. The addition of seventy-five case histories helps to elucidate the way in which the author puts his ideas into practice. Dr. Dennett is a strong advocate of the value of boiling milk, and he brings forward his experience on this phase of infant-feeding with much force of argument, which gives the work an unmistakable personal tone.

The chapter on proprietary foods brings together in one place, ready for reference, the analyses of these various foods, so that the busy practitioner may easily ascertain what any child may have been getting who has previously been fed on foods of this nature.

J. F. S.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF
W. S. THAYER, M.D.,
PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,
AND
ROGER S. MORRIS, M.D.,
FREDERICK FORCHHEIMER PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO.

Vaccine Therapy of Typhoid Fever.—MEYER (*Berl. klin. Wchnschr.*, 1915, lii, 677) reports favorable results in 62 cases of severe typhoid fever treated by vaccine therapy. He found that the intravenous injection of a sensitized vaccine in the later stages of typhoid particularly tended to develop immunity. He believes that these injections are especially useful when applied during convalescence to prevent relapses and late sequelæ of typhoid fever.

Specific Treatment of the Malignant Forms of Malaria.—BASS (*Jour. Amer. Med. Assn.*, 1915, lxv, 577) says that the proper specific treatment of malignant or pernicious malaria is quinin administered intravenously. The dose and method of administering quinin intravenously are important. Bass does not believe that it is ever necessary to exceed 30 grains of quinin hydrochlorid during twenty-four hours when administered intravenously. He emphasizes the point that a single dose should never exceed 10 grains of the hydrochlorid. Large doses of quinin given intravenously are very dangerous. Twenty grains often produce considerable shock, dizziness, nausea, etc., and a dose of 50 grains has killed in several instances. Bass believes that 10 grains of quinin hydrochlorid given intravenously every eight hours or 5 grains every four hours will kill plasmodia in the blood stream and prevent their reproduction as certainly as any larger quantity and will not endanger the life of the patient. The author discusses briefly the subject of malarial hemoglobinuria. In malarial hemoglobinuria, red cells containing plasmodia, and thus damaged, are affected more certainly and more extensively than the normal cells. As a result they are hemolyzed, leaving the plasmodia they contained exposed to the plasma, which promptly destroys them. The only object of giving quinin in malaria is to destroy plasmodia, and if most or all of the plasmodia have disappeared, which is the case in hemoglobinuria, there is no indication for quinin. There is a certain amount of contra-indication, however, because quinin tends to increase hemoglobinuria or to precipitate attacks in otherwise susceptible individuals.

Contribution to the Pathology of the Blood in Chronic Lead Poisoning.—Sehnitter (*Deutsch. Arch. f. klin. Med.*, 1915, cxvii) draws the following conclusions after studying the blood of 196 cases of lead poisoning: (1) Basophilic stippling of the red cells is always present in chronic cases. (2) There is no constant relation between the degree of blood changes and the severity of the clinical manifestations. In general, however, they are roughly parallel. (3) The anemia present is most apt to be of the chlorotic type. (4) In a progressive intoxication, polychromatophilia appears first, followed by stippling. As the poisoning progresses, anisocytosis and reduction in the number of red cells may become very marked and is frequently associated with varying numbers of normoblasts, which may occasionally occur in crises. (5) A completely aplastic blood picture, such as is seen in benzol poisoning almost never occurs. (6) Most cases are associated with a moderate leukocytosis, which indicates a better prognosis than in those associated with a leukopenia. (7) The differential count shows a lymphocytic increase which may include the large mononuclear and transitional cells. The platelets are usually enormously increased. (8) Severe blood changes require six months to a year for complete restoration.

The Estimation of the Rest N. in the Blood as a Method of Testing Renal Function.—H. Hohlweg (*Mitt. a. d. Grenzeb. d. Med. u. Chir.*, 1915, xxviii, 459), in association with Meyer, was among the first to demonstrate the value of determining the rest N. of the serum in the diagnosis and prognosis of severe nephritis. In the present communication, he reports observations on the rest N. of the serum of patients with uni- and bilateral kidney disease, before and after operation. He found normal values in pure unilateral disease and no increase following nephrectomy if the remaining kidney was normal. In patients with one diseased kidney and a toxic injury in the other, the rest N. is increased. Values up to 75 mg. for 100 c.c. of serum do not contra-indicate operation and in general indicate that the process in the good side is still reparable, or at least capable of improvement. Values of 100 mg. contra-indicate operation. The rest N. may increase just after operation but in four to six weeks it returns to its original level and may go lower than normal.

The Value of Uric Acid Determinations in the Blood.—Within recent years Brugsch and Schittenhelm have asserted that normal blood contains no uric acid. Its presence they consider as pointing to the existence of gout. Folin and Denis (*Arch. Int. Med.*, 1915, xvi, 33) point out the fallacy of Brugsch's clinical method for the demonstration of uric acid by means of the well-known phosphotungstic acid reagent. It should be remembered that all blood contains varying amounts of phenols which also give a blue color with the above reagent, in fact in some cases the amount of color produced may be two or three times greater than that given by the uric acid present in the blood. Folin and Denis are convinced that all short-cut methods so far proposed for the clinical determination of the uric acid in the blood are bound to give grossly misleading results. They have found by their method that normally uric acid is present in from 1.5 to 2.5 mg. per hundred cubic centimeters, and that in gout, lead poisoning, leukemia and some cases of nephritis, these amounts may be greatly increased. As a result of their study of several hundred uric acid determinations, made on many different kinds of human blood, Folin and Denis have become convinced that even exact quantitative uric acid determinations are not by themselves an adequate protection against frequent mistakes in the differential diagnosis of gout and other joint diseases. From tables which accompany the present article it will be seen that to be of material help in the differential diagnosis of gout, the uric acid determinations must be accompanied by determinations of the non-protein nitrogen. For any joint disease other than gout it is by no means uncommon to find uric acid values nearly, if not quite, so high as in gout. In arthritis, however, a high non-protein nitrogen is more frequent than a high uric acid, thus resembling frequently the blood from a case of glomerular nephritis. In addition to the determination of the uric acid and non-protein nitrogen, the patient must be put on a purin-free diet for at least two days before blood is withdrawn for analytical purposes.

Clinical Value of Diastolic Blood-pressure Determinations.—WARFIELD (*New York Med. Jour.*, 1915, cii, 509) is of the opinion that far too little importance is generally attached to the determination of the diastolic blood-pressure, and emphasizes the fact that pressure determinations in general, to be of any real value, should always include the systolic, diastolic and pulse pressure. These three constitute what he chooses to term the "pressure picture." After a brief discussion of the various opinions regarding the exact time at which the diastolic pressure should be read by the auscultatory method, Warfield points out the following clinical facts in support of his contention that the estimation of the diastolic pressure is more important than that of the systolic: (1) The diastolic pressure is more constant in individuals than the systolic. (2) Since it measures peripheral resistance, it would seem to be a more accurate index of either high or low tension than the systolic pressure. (3) A gradually rising diastolic pressure is of more significance than high systolic pressure. (4) Pulse pressure can only be accurately determined when the diastolic pressure is carefully measured. Large pulse pressures are apparently essential for the compensation of hypertension cases, while falling pulse pressures in such cases, indicate a failing heart. A pulse pressure below 30 mm. of mercury must be regarded as low, those above 50 as high. (5) The diastolic pressure should be taken by the auscultatory method at the sudden transition from the loud third tone to the dull fourth tone. Since the disappearance of all sound so closely follows the fourth tone, the diastolic pressure can safely be taken at that point. (6) Accurate determination of either systolic or diastolic pressure cannot be made upon decompensating hearts.

Our Present Knowledge Concerning Leprosy.—McCoy (*Am. Jour. Trop. Dis. and Prev. Med.*, 1915, iii, 83) says that the organism described by Kedrowski fifteen years ago, and believed to be the cause of leprosy, has been cultivated by a great many observers and in a variety of different ways. In addition to this acid-fast bacillus, diphtheroid organisms have been grown so many times from leprous tissues that the relationship of this group to the bacteria of the disease in question still demands an explanation. A tremendous number of attempts to reproduce the disease in lower animals have been futile. Indeed some 50 instances in which human bodies have been inoculated with leprous tissue tend to prove that this is an entirely safe procedure. This failure to produce an undoubtedly infectious disease with the acid-fast bacillus of leprosy, has naturally led to the suspicion that some other organism is the causative agent, but as yet it has not been demonstrated. There exists no support of Hutchinson's theory of the relation of the disease to fish-eating. Complement-fixation tests are generally positive and specific when the sera of the lepers are tested against antigens prepared from extracts of lepromas. The same sera very frequently bind complement when tuberculin is used as an antigen; finally, between 40 and 90 per cent. of all lepers give a positive Wassermann reaction, though they consistently give negative results with Noguchi's luetin test. All of these biological reactions are most pronounced in cases of the nodular type. At the present time we are still in ignorance as to how the disease is conveyed from person to person, or where the organism sojourns outside the human host. The bacillus doubtless escapes through open lesions of the skin and mucous membranes, but is probably never present in any of the excretions or secretions of the body. Healthy "nasal carriers" have been repeatedly observed. The studies of Hollmann go far toward disclaiming the role of heredity in the etiology of this disease. No positive diagnosis of leprosy should be made without the aid of microscopic examination of some of the tissues. Vaccine and antisera have thus far been of little value in treatment. Practically the only remedy giving favorable results is chaulmoogra oil. It is doubtful if any cases are ever cured. The protection of the community practically resolves itself into segregation of the afflicted.

The Lymphocyte and Natural and Induced Resistance to Transplanted Cancer.—Murphy and Morton (*Jour. Exper. Med.*, 1915, xxii, 204) report the results of their observations on the changes in the number of circulating lymphocytes in experimental carcinoma in mice, and the relation of this lymphocytosis to immunity. The basis for these observations appear in earlier communications in which the authors noted that adult animals deprived of most of their lymphoid system by Roentgen rays, no longer resisted the growth of heterologous tissues. The animals were divided into three groups: (*a*) Those having a natural immunity. (*b*) Those in which immunity was induced by the subcutaneous or intraperitoneal injections of a small amount of homologous living tissue at least ten days before inoculating the cancer graft. (*c*) Susceptible animals not naturally immune nor rendered so by previous treatment. In the first two groups (*a* and *b*), a definite lymphoid crisis occurs in the circulating blood within twenty-four hours after the introduction of the cancer graft which does not take. In control animals in which the tumor grows, there is no such lymphoid response, while the polynuclear cells show a tendency to increase. Additional experiments show that this lymphoid reaction is not merely an accompanying factor in the immune period, but is essential to it. This is shown by the fact that destruction of the lymphocytes by Roentgen rays causes a loss of this natural or acquired immunity, thus rendering these animals susceptible to the tumor graft. In these cases, of course, there is no lymphoid response following the inoculation.

SURGERY

UNDER THE CHARGE OF

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The Immediate and Late Disturbances from Kulenkampff's Anesthesia by Injection of the Brachial Plexus.—Schepelmann (*Deutsch. Ztschr. f. Chir.*, 1915, cxxx, 558) says that during the past year and a half he has anesthetized the upper extremity by Kulenkampff's method in 300 cases and among harmless symptoms, has observed many times, arising suddenly, very disturbing symptoms which deserve consideration. Kulenkampff's technic was followed closely. By experimentation on rabbits Schepelmann found that injection of large doses of sinecain, cocain, or novocain, produced very severe cerebral symptoms. In cadavers he injected the brachial plexus with a methylene blue solution and found that by injecting exactly into the nerve sheath, the methylene blue extended itself under the spinal dura mater upward and downward over wide distances, many times upward as far as the brain. Aside from the harmless Horner symptom-complex (contraction of the lid-cleft and pupil of the same side, sinking backward of the eyeball, redness and sensitiveness of the conjunctiva), there were observed in 4 of the 300 cases more or less marked dyspnea in consequence of injuries of the pleura. In one case pneumothorax developed and twice, at first, alarming but transitory cerebral disturbances. Altogether there were 7 cases in connection with which disagreeable immediate effects were recorded. If, however, narcosis had been substituted for this method, at least, as many cases with disagreeable disturbances would have been met among patients with recent wounds calling for anesthesia without a preliminary preparation of the gastro-intestinal tract. The Kulenkampff method should not be employed where milder local anesthetic methods would suffice. It should be employed, however, where these methods are not sufficient, as in extensive suppurations and inflammations, major operations on the hands and arms, reduction of fractures and dislocations, and in amputations and excisions. It is especially desirable when Esmarch's method of hemostasis is employed. On the other hand, Schepelmann regards the double-sided plexus anesthesia as an unjustifiable procedure, because of the possibility of wounding both phrenic nerves, pleural cavities and lungs and thereby inducing very severe or fatal results. He has not observed any evil effects from frequent repetition of the plexus anesthesia at intervals of about eight days. A puncture of the subclavian artery with a fine needle is not considered serious, while the subclavian vein is too deep to be injured.

Comparison of the Secretion of the Two Kidneys in Dogs.—Lepine and Boulud (*Jour. d'urolog.*, 1915, vi, 297) made a study on dogs of the comparative excretion of the two kidneys. They did not find, as maintained by some writers, that the secretion of the two kidneys balance each other. The average for the right was somewhat greater than for the left, but when the dogs were perfectly normal the difference between the two sides was not marked. If one kidney is secreting against a moderate counter-pressure (30 to 40 c.c. of water), the quantity of water and chlorides excreted during this counter-pressure is sensibly less than on the opposite side where the escape is free. This diminution is due in part to an increase of the intrarenal absorption of water and chlorides. Consecutively, to an obstruction of one ureter of less than fifteen hours' duration, the water and chlorides are excreted in relatively greater abundance because of the diminution of the absorption by the functionally altered kidney. Unilateral intoxication of a kidney by the penetration of a few cubic centimeters of saline solution with the addition of quinin sulphate in the proportion of four parts to a thousand, produces a chloruria which may be excessive and is explained by a great diminution of the intrarenal absorption of the chlorides.

Gall-stone Disease.—Deaver (*Ann. Surg.*, 1915, lxii, 197) reviews the case records of gall-stone disease operated on in his clinic at the German Hospital during the year 1914. The cases presented numbered 159, 87 of which are classified as simple gall-bladder disease, including types of cholecystitis with or without stones; 20 cases of gall-bladder and common duct involvement; 52 cases of gall-bladder disease with secondary pancreatic involvement, and 7 reoperative cases. Gall-bladder disease is preëminently a disease of the middle-aged female, but is by no means confined to that age or sex. The early diagnosis can be made only by familiarity with a different symptomatology than that found in the text-books. The lighter grades of dyspepsia with localizing signs, however slight, in the epigastrium or right hypochondrium must be regarded as very suspicious of the beginnings of gall-stone disease. Infection as the cause, not only of gall-stones, but of the local and systemic damage of the disease, is the essential thing to recognize and treat. The Roentgen-ray in diagnosis is dangerous, not only because it fails to show a large percentage of stones, but because it emphasizes the importance of the calculous element of the disease, and if allowed to serve as an indication for operation will deprive many of the early treatment which alone is safe and efficacious. Cholecystectomy is the operation of choice in obviously diseased gallbladders, with drainage of the common duct in practically all cases, but particularly in those giving evidence of cholangitis or pancreatic involvement.

Paget's Disease of the Nipple and Allied Conditions.—Jopson and Speese (*Ann. Surg.*, 1915, lxii, 212) say that Paget's disease of the nipple is a primary affection beginning in the cells of the rete Malpighii potentially malignant, although lacking the ordinary characteristics of malignant disease. It is identical with the disease known under the name of Paget occurring in other regions. It is commonly, although not invariably, followed by glandular carcinoma in the underlying breast tissue. It is precancerous in the sense that it induces epithelial changes in the superficial milk ducts and acini, which are followed by carcinoma. Occasionally, although rarely, it is followed by squamous cell carcinoma of the nipple. The disease is characterized by edema and vacuolization of the prickle cells, thickening of the rete, and active mitosis, also by an inflammatory reaction in the corium and a secondary hyperplasia in the milk ducts. It is sharply differentiated from true eczema and scirrhus carcinoma ulcerating at the nipple, and should not be confused with superficial metastases of diffuse cancer situated near the skin. The resulting tumors of the breast and the regional metastases resemble the type of breast cancer usually encountered. When the tumor originates in the skin, it infiltrates and metastasizes in the form of squamous carcinoma. The common association of cancer in the breast with Paget's disease demands as the treatment for Paget's disease the radical operation which is practised in breast cancers in general.

Second Report of the Committee on the Treatment of Structural Scoliosis to the American Orthopedic Association.—(*Amer. Jour. Orthop. Surg.*, 1915, xiii, 6). The committee offers the following summary as the result of its investigation of a second series of cases: (1) No case of overcorrection of the elements of deformity in structural scoliosis has been presented to the Committee, in which they have been permitted to observe and record the condition of the patient from a time preceding the beginning of treatment. (2) The time allowed by the Committee has been sufficient, in their judgment, for such a demonstration, were it possible in the respective patients and by the respective methods. (3) The same statements may be made with respect to complete correction of the elements of the deformity. (4) The amount of correction demonstrated to the Committee by means of the method of Forbes is unsatisfactory and is to be regarded as entirely insufficient reward for the amount of labor, discomfort and other inconvenience which is involved. (5) In mild cases of undoubtedly structural scoliosis, and perhaps in some moderately severe cases, considerable degrees of correction may be achieved by means of the method of Lovett and and by Kleinberg's brace. (6) It seems probably that greater degrees of correction may be obtained with the flexed position of the spine than with the extended position of the spine. (7) It does not appear that the use of extreme force is justified by the results which are to be obtained from it. (8) In order to have reciprocal application to the given case, all records should be made with the patient in the same position; this refers to the clinical, photographic and roentgenographic record and to the horizontal or upright position of the patient. (9) For purposes of record the upright position is to be preferred.

Radium Treatment of Inoperable Uterine Cancer.—A report upon this subject recently published by Newcomet (*New York Med. Jour.*, 1915, cii, 19) strikes a decidedly pessimistic note, at least so far as any results that can be shown are concerned. Whether this may be due to to the rather small amounts of radium used (10 to 40 mg.) the author does not state. The paper is based on the last 50 consecutive cases of uterine carcinoma treated at the Oncologic Hospital, Philadelphia. Unfortunately no distinction is made between cervical and fundal cancer. About half the patients were under forty-five years of age; all were in more or less advanced stages of the disease, the condition being practically inoperable in most of them. In not a few instances the operable stage had been passed, not from any neglect or unwillingness of the patient to undergo operation, but because the symptoms were so slight as not to attract the woman's attention. In 3 cases the condition followed so closely upon a recent labor that the bleeding was considered merely a lochial discharge, while in one the first warning of anything wrong was the passage of fecal matter through the vaginal fistula. The 50 cases are classified into the following six groups: (1) Patients who left the hospital while under treatment, 4 cases. (2) Still under treatment, 2 cases. (3) Died while under treatment or subsequent observation, 14 cases. In most of these, death occurred within a few months of coming under treatment, and in all the disease apparently followed its natural course, uninfluenced by the radiation. (4) Unimproved, 24 cases; these patients have left the institution and have ben lost sight of; probably most of them are dead. (5) Improved, 11 cases; while in many instances the improvement was temporary, these patients did at least get some apparent relief for a time. (6) Greatly improved, 5 cases; in these the disease process diappeared, and was not detectable upon local examination; only one of these was an unoperated case, however; this was a woman, aged seventy years, with a very slow growing type of carcinoma; the other four had early recurrences following operation. The hemostatic action of radium, which has been so much insisted upon by almost all writers, was seen in most instances, but two women died of sudden violent hemorrhage coming on within a month or six weeks from cessation of treatment. In some instances there was relief of pain, but in a large proportion no influence of this kind could be noted, and some patients even complained of increased pain after exposure to radium. A number showed increased mental excitement, loss of sleep, and in three instances acute mania developed. The technique consisted in the introduction of a metal capsule containing the radium into the vagina for from three to eight hours daily, every other day, or at longer intervals, the duration frequency of treatments being governed by the amount of reaction obtained. Burning was always avoided, and no sloughing ulcers were produced.

THERAPEUTICS

UNDER THE CHARGE OF

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Salvarsannatrium.—Gutmann (*Berl. klin. Wchnschr.*, 1915, lii, 400) writes concerning salvarsannatrium, which is a derivative of old salvarsan, so prepared that when dissolved in distilled water, its solution have the same chemical composition as solutions of old salvarsan prepared in the ordinary way by neutralization with sodium hydrate. The chief advantage of salvarsannatrium is the great simplicity of the technique of preparing the solution for injection, the new preparation being as easily soluble in water as is neosalvarsan. It is claimed, therefore, that salvarsannatrium combines the advantages of simple technique of administration of neosalvarsan while retaining the full therapeutic effect of old salvarsan. Salvarsannatrium is a yellowish powder which oxidizes readily on exposure to the air. The oxidized product is markedly toxic and, for this reason, solutions for injection must be made immediately before using. Gutmann recommends the method of Dreyfus who advises dissolving the dose in 20 to 30 c.c. of doubly distilled sterile water and injecting this intravenously by the syringe method. Gutmann advises a dose of 0.6 gm. for men and 0.45 gm. for women. During a period of six or seven weeks' treatment from 4 to 6 gm. can be given without untoward symptoms. A rise of temperature usually follows the intravenous injection. This promptly subsides and cannot be avoided. Skin eruptions of various types have also occasionally followed salvarsannatrium injections but are of short duration. No serious untoward symptoms have followed the use of salvarsannatrium in Gutmann's experience.

Immediate Results of Splenectomy in Pernicious Anemia.—Lee, Vincent, and Robertson (*Jour. Amer. Med. Assn.*, 1915, lxv, 216) report a series of 5 cases of pernicious anemia treated by splenectomy. The immediate results in this series were a prompt postoperative recovery and a definite remission of the disease in every case. The remissions were much more marked than are usually seen in pernicious anemia. In 4 of the 5 cases the red blood cells rose to from 4,000,000 to 5,000,000. However, in spite of the marked improvement, the blood picture retained the characteristics of pernicious anemia with the exception of a change in the color index from high to normal or low. Furthermore, in 3 of the 5 cases, evidence of increased blood destruction was present several months after splenectomy, as shown by the urobilin estimation. The authors cannot state that the improvement following splenectomy will last longer than the remissions which come spontaneously, and which may persist over a period of years. The only conclusions which the authors are willing to draw from the cases reported by them combined with the reports of other writers are: (1) Splenectomy is not a very serious operation in pernicious anemia, and it offers a definite means of inducing a remission. (2) The remission thus brought about is more marked in the majority of the cases than any other known therapeutic procedure.

Recent Experiences in Vaccine Treatment.—Madden (*Lancet, London,* 1915, clxxxix, 267) prefers to use an autogenous vaccine, as a more potent and direct vaccine is made available. The strength of vaccine is generally 250 million to 1 c.c., with an initial dose of 50 million. The interval between the doses depend upon the case itself and the reaction produced, but they are never less than five days. The general effect of an appropriate vaccine, according to Madden, is to produce a definite reaction with fever and malaise and usually also a distinct but temporary exacerbation of the symptoms of the condition under treatment. When this degree of reaction occurs the injection should be carried steadily on in increasing strengths at proper intervals. The maximum curative effect is generally gained in from 8 to 12 injections. Madden has employed vaccines systematically in the treatment of boils and furunculosis generally. So universally successful has this method been in his hands that he never employs any other. A start is made with 100 million followed by 500 million five days later, and at a similar interval by 1000 million. Generally this series of three injections suffices to cure in the ordinary case; but in more intractable cases a further series working rapidly up to 5000 million, will almost certainly be sufficient. He has also had some success in cases of pyorrhea alveolaris with an autogenous vaccine, but he advises that vigorous local treatment must be carried out at the same time. In acne the results have been on the whole very disappointing. Compartively recent and uncomplicated pustular acne does, however, react very promptly in almost the same degree as an inverterate furunculosis; but in old cases, in which there is much scarring about the sebaceous follicles, results are likely to be disappointing. A further very important use of vaccines, Madden says, is in boils, carbuncles, and cellulitis occurring in diabetes. Here particularly one must make a practice of giving large and repeated doses of vaccines, alternating in extreme cases with antistreptococcic serums. Septic infection from operation wound or injury may also be controlled by vaccines; but it is very necessary to make sure of the causal organism before beginning a series of injections. Madden points out that in all vaccine treatment it must be remembered that an incision into the affected part acts like a vaccine, as it produces a phagocytosis which will itself have a vaccinal effect; quite apart from the evacuation of pus and septic serum and the relief of tension by the incision. Care must therefore be taken not to give a strong dose of a vaccine at the same time as the incision or too violent a reaction may occur. Further, vaccine must not be given during the stage of depression or of anaphylaxis resulting from the vaccinal effect of the incision. Madden states that he knows of no better treatment for infection of the urinary tract due to colon bacilli than that by vaccines, although treatment has to be long continued and relapse may occur. With respect to vaccine treatment of gonorrhea and its complications he has found that results have been very disappointing when the gonococcus infecting organism. Certain cases of mixed infection respond to the is the principal proper vaccines. Pneumococcic vaccine, either as stock for acute lobar pneumonia or as an autogenous vaccine in cases of old chronic cough, especially if consequent upon a former inflammation of the lungs, is most useful but should not be depended upon entirely.

The Use of Digitalis in Various Forms of Cardiac Arrhythmia.—Christian (*Bost. Med. and Surg. Jour.*, 1915, clxxiii, 306) says that an important indication of the beneficial action of digitalis is the decrease in the pulse deficit, *i. e.*, the difference between the apex beat and the radial pulse. In auricular fibrillation the counting of the radial pulse may be very misleading, it often being within normal limits when actually the heart is beating very rapidly. Digitalis impedes conduction in the bundle of His, and the result is that fewer auricular contractions send impulses through to originate ventricular contractions and consequently the ventricle beats more slowly. With slower contraction of the ventricle, there is more time for the ventricle to fill and more time for the muscle to recover from fatigue. Digitalis also probably exerts an action on the myocardium, causing more forcible contractions, and improves coronary circulation. In some patients with auricular fibrillation in which edema is marked, a much better diuresis is obtained by combining with the digitalis a diuretic drug, such as theocin. In another form of arrhythmia, namely, auricular flutter, digitalis usually produces a striking effect. The heart in such cases may slow down directly into a normal rhythm with great improvement in the patient's condition, or the digitalis may throw the auricle into fibrillation and when digitalis is stopped the normal rhythm is restored. In pulsus alternans digitalis frequently produces good results. In the rapid, regular, decompensated heart digitalis slows the rate by increasing vagus inhibition and by increasing conduction time between auricle and ventricle, and it strengthens heart action by some direct action on the myocardium and coronary circulation. This type of case often seems definitely resistant to digitalis and the patient may take large amounts before any effect can be detected. It is always well to remember in such cases to watch the patient carefully for sometimes the digitalis action, which has been long delayed, develops with great rapidity into marked activity so that the patient, who shortly before has shown no digitalis effect, quickly develops toxic symptoms. In paroxysmal tachycardia there is little evidence that digitalis produces any good effect. In sinus arrhythmia and in compensated hearts with ectopic beats or extrasystoles digitalis is not indicated. In cases of heart block not of digitalis origin, digitalis should be tried if the patient is decompensated. Results are sometimes good; at other times it would seem that the patient is made worse. Christian advocates the selection of one good digitalis preparation for administration by mouth and one for intravenous use. By continued use of the same preparations it is easier to estimate in a given case whether digitalis is effective or not. He deprecates the great number of "improved" preparations of digitalis as too confusing for proper judgment of effects. He prefers to use powdered digitalis or a freshly made infusion for oral administration and liquid digipuratum for intravenous use. Occasionally strophanthin intravenously is indicated but due regard must be paid to the necessary caution against strophanthin in a patient who has been taking digitalis by mouth. As to dosage Christian says that relatively large doses should be used in periods of decomposition. With compensation restored very small doses continued over long periods certainly seem to be of great help in maintaining compensation.

The Inactivation of Pepsin by Sodium Chloride; Its Clinical Significance.—HAMBURGER (*Arch. Int. Med.*, 1915, xvi, 356) describes experiments that constantly showed that the neutralization of gastric juice results in complete inhibition of peptic action even after the addition of hydrochloric acid in excess, and that the inhibition of pepsin is due to sodium chloride acting in a neutral medium. The clinical application of these findings would lie in the ability to adapt measures whereby the stomach acid could be completely neutralized and the neutral reaction continuously maintained, and also that the newly formed and secreted acid could be immediately and continuously bound with alkali as soon as it was formed. If this could be accomplished, the pepsin set free by neutralization, as well as the newly secreted pepsin, would be bound by inhibiting sodium chloride and permanently inactivated. As a result, peptic activity would be destroyed for a period of time equal to the continuance of the neutral reaction, a condition similar to achylia gastrica. Such a temporary achylia would be desirable: (1) as a prophylactic measure, to prevent the formation of gastric or duodenal ulcer; (2) to facilitate the healing of ulcer by removing the factor which, next to mechanical trauma, is probably of greatest importance in the continuance and progression of chronic ulcer. Therefore in simple hyperacidity, in hypersecretion from whatever cause, in motor insufficiency with continuous secretion, in pylorospasm with hyperacidity and hypersecretion, in chronic ulcer, in gastro-enterostomy to prevent the formation of jejunal ulcer. Neutralization with peptic inactivation might be desired. The author states that by the use and combination of certain alkalies with certain foods and methods of feeding, continuous and complete neutralization of the stomach contents can be maintained.

The Treatment of Heart Disease.—SHATTUCK (*Bost. Med. and Surg. Jour.*, 1915, clxxiii, 316) presents the general principles of the treatment and management of patients suffering from cardiac disease with especial reference to the treatment of angina. He emphasizes that the all-important therapy of angina, whether grave or relatively benign, is the regulation of the mode of life. Every effort should be made to avoid bringing on pain. Shattuck points out that the details of medicinal treatment of true angina depend somewhat on its origin—whether this be infectious or non-infectious, and if infectious whether of syphilitic or other origin. Medicinal treatment is usually of minor, though still of real importance. Strychnia is to be avoided as tending to heighten reflex excitability. Digitalis is indicated only so far as myocardial failure is suggested by symptoms other than pain. Small doses of potassium iodid can seldom be harmful and seem to be of value even in non-syphilitic cases. The action of glonoin is so transitory that its value between attacks is doubtful. If it be desirable, as Shattuck believes to be rarely the case, to try to secure constant reduction of blood pressure, sodium nitrite or erythrol may be used.

PEDIATRICS

UNDER THE CHARGE OF

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Camphor Abscess.—Vogt (*Monatschr. f. Kinderh.*, 1915, xiii, 381) reports the great frequency of abscesses following the subcutaneous injection of camphor-oil in sick children in the pediatric wards of a hospital in Magdeburg. He mentions the possibility of some peculiar constitutional condition of the children of that part of the country making them more susceptible to the development of such lesions than the children of other parts of the Empire. These abscesses were so frequent that the technique of the subcutaneous injection, the asepsis and the material used was inspected and regulated with the utmost thoroughness, with no result in the diminution of the number of abscesses resulting. Also the abscesses were found for the most part to be sterile, a very few showing organisms which proved to be mostly staphylococci. The larger abscesses, even though sterile prove an unfavorable factor in seriously ill children. Abscesses opened during life or at autopsy showed the camphoric odor and large quantities of oil-droplets to have persisted a long time after the injection. It would then appear that the oil produced an irritation in the tissues and by remaining there for a long time acted as a foreign body. Camphor itself has irritating properties and causes locally more or less pain with subsequent redness and inflammation. It is noteworthy that the many injections of digalin and caffein employed in these cases resulted very rarely in abscess formation. In the development of abscess in the various cases there was apparently no relation the state of nutrition, the amount of subcutaneous fat, the severity of the general condition or the presence of edema. From this experiment it would seem that under certain conditions the subcutaneous injection of camphor may be attended by serious injury.

Clinical Distinctions between Cerebral Intoxication, Meningism, and Meningitis.—Heiman (*Arch. Pediat.*, 1915, xxxii, 579) discusses the clinical distinctions between meningitis and conditions with which it is often confused. Cerebral intoxication is a condition produced by absorbtion of toxins from physicochemical or bacterial agents or from animal or vegetable matter and characterized by irritative phenomena such as delirium, involuntary muscular movements, etc., and is fairly frequent in severe infections. Meningism, so-called serous meningitis, is a morbid process resembling meningitis in its manifestations but in which the spinal fluid is sterile. Cerebral intoxication is most strikingly illustrated in severe cases of pneumonia and typhoid fever, with delirium, photophobia, retraction and rigidity of the neck and twitching of the muscles or convulsion. Autopsy generally shows no lesions of the cerebrospinal system. There is always an etiologic factor to which the meningeal signs are secondary and the signs are significant of a general cerebral irritation, while primary meningitis offers in addition focal signs, ptosis of the eyelids, strabismus, unequal pupils, etc. Lumbar puncture in intoxication shows the fluid sterile and clear with no variation from the normal cytological count while in meningitis various changes are present from the normal. Meningism indicates a greater degree of cerebral toxemia than is shown in cerebral intoxication and differs only by exhibiting increased intracranial pressure and a symptom-complex which still more simulates true meningitis. Its causes may be classified as infectious or toxic, irritative, reflex and hysterical. Under the first head acidosis and the later stages of gastrointeritis are most frequent causes. Of irritative causes head injuries, subacute and chronic ear conditions, and operations on the cranium, are found. Helminthiasis is included as a possible factor under reflex causes, and the hysterical types are cases claimed by the French to be occasionally mistaken for tuberculous meningitis. In meningism there is an etiological factor, the symptoms are transitory and subside with improvement in the etiological condition. The ophalmoscopic findings are negative and ocular changes rare, a slight congestion of the disks occasionally ocurring. The bacteriological and cytological differences in the spinal fluid must, of course, be regarded as the most important differential signs.

The Sex Distribution of Rickets.—Priestly (*Brit. Jour. Child. Dis.*, 1915, xii, 173) reports several studies made during routine medical inspection in schools to determine the sex distribution in rickets. The total numbers of cases were rather constant from year to year, being 0.25 to 0.14 per cent. during the last five years. Out of a total number of boys and girls examined, 75,000, rickets appeared in boys 2.04 per cent., and in girls 1.13 per cent. This shows a difference in the incidence of rickets or rather post-rickety deformities, between boys and girls which is not quite in ratio of 2 : 1. In minor cases of rickets the same general effect is observed and in observing 5000 cases the boys were found to have 27 per cent. and the girls 16 per cent. The disease therefore seems more prevalent in boys than in girls, and should be included with rheumatism, pulmonary tuberculosis, and the graver nervous affections among the diseases whose incidence is considerably influenced by sex.

Aborted Pneumonia and Mistreatment of Pneumonia.—Epstein (*Pediatrics*, 1915, xxvii, 70) criticizes the frequent diagnosis, "A touch of pneumonia," made by some physicians. A lobar pneumonia may be of short duration either because the different pathological stages are shorter or because the pneumonia terminates without passing through all the stages. These short pneumonias are rare and above the diagnostic ability of the average physician. Usually an "aborted pneumonia" is really some other known or unknown infection. Much is written on the treatment of pneumonia, but little is said of the mistreatment of the disease. As there is no specific treatment for the pneumonia the patient should be mainly treated and not the disease. Mistreatment consists of either too little attention, as in giving an ultrahomeopathic dose of some medicine and neglecting the patient, or in over-medication with all kinds of irritating drugs and nauseating syrups, such as ammonium carbonate, etc. The best treatment is to conserve the child's strength and energy and to combat unfavorable symptoms. Hydrotherapy, proper feeding and plenty of fresh air with a temperature not too low in asthenic cases is of prime importance. The drug treatment can be divided into three classes—catharsis, diuresis and diaphoresis, and cardiorespiratory stimulation.

A Clinical and Pathological Study of 100 Infants.—SMITH and COBB (*Archiv. Pediat.*, 1915, xxxii, 434) present the data of two summer's work on the Boston Floating Hospital. The pathological findings represent a check on the clinical diagnosis of the various groups studied. Three main groups of digestive disturbances are noted as indigestion, indigestion with fermentation, and infectious diarrhea. Indigestion is from overfeeding of some food element or errors in feeding and the majority of cases recover. The autopsy findings in 25 cases of this group showed the gastro-intestinal tract normal in one-half the cases with the other half showing conditions from marked congestion to follicular and ulcerative enterocolitis. In the group called "indigestion with fermentation" the etiology is not clear, probably simple digestive disturbance and an infection enter into the condition which is of short duration, marked prostration and green, mucous or bloody stools. Of the 7 cases of this group coming to autopsy the majority showed nothing more advanced than congestion or catarrhal inflammation; only 1 case showing necrosis. In the third group, "infectious diarrhea," the etiology is bacterial, the clinical picture is the same for different organisms and the symptoms are of two types, digestive such as vomiting and diarrhea, and toxic, as high fever and prostration. In infection by the Flexner bacillus lactose solution is favorably employed, but in infection by the gas bacillus, feeding high proteid and low carbohydrates, as lactic acid milk is more favorable. Of the 40 cases coming to autopsy in this group 17 had follicular enterocolitis with necrosis, 9 had ulcerative enterocolitis or typical dysentery, and 7 had membranous enterocolitis, showing that the severe types of lesion predominate.

The Gas Bacillus and Infectious Diarrhea in Childhood.—SYLVESTER and HIBBEN (*Archiv. Pediat.*, 1915, xxxii, 457) describe their investigation of digestive disturbances caused by the gas bacillus and the treatment based on scientific study. Their investigation embraced infectious diarrhea, fat intolerance, carbohydrate intolerance, and chronic intestinal indigestion (marasmus). The test for the gas bacillus was based on the gas-forming properties of the bacillus in a carbohydrate media at suitable temperature and was therefore either positive or negative in any one case. The number of cases investigated were 172, of which 100 were positive and 72 negative. Infectious diarrhea showed 38 cases positive and 9 negative. Fat intolerance, 29 positive, 3 negative. Carbohydrate intolerance, 3 positive. Acute intestinal indigestion, 5 positive, 2 negative. Chronic intestinal indigestion, 15 positive, 4 negative. Breast-fed children under two weeks old, none positive, 30 negative. Controls made at frequent intervals showed that tap water, throat sticks and soap used for suppositories were uniformly negative. The Bacillus aërogenes capsulatus is generally distributed in soil, milk and sewage, but is not a normal inhabitant of the intestinal tract of healthy breast-fed infants, nor was it found in 30 breast-fed infants under two weeks of age examined by Sylvester and Hibben. The gas bacillus grows luxuriantly on a high carbohydrate medicine and lactic acid is inimical to its growth and reproduction. It is advised in the treatment of these disorders to give a 5 per cent. lactose solution until a positive diagnosis is made of the presence of the gas bacillus by bacteriological examination. If the diagnosis is positive for gas bacillus unpasteurized, fat-free lactic acid milk is given and all carbohydrates are withdrawn. This is preferred to the administration of lactic acid bacilli culture.

OBSTETRICS

UNDER THE CHARGE OF

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Birth Palsy.—Platt (*Brit. Med. Jour.*, May 8, 1915) states that there are two theories to explain birth palsy. In one the paralysis is primarily due to stretching or tearing of the brachial plexus, by the other theory the primary lesion is one of the joints or bones, and the nervous lesions and symptoms are secondary. The cases usually follow a difficult labor, one arm of the infant hanging limp and motionless. The arm hangs close to the side with internal rotation at the shoulder, the elbow extended, the forearm pronated, fingers flexed and sometimes wrist-drop. The neck and shoulder may be tender for a few days. In many cases rapid and complete recovery follows, rarely no recovery or arm remaining practically useless, while in a considerable number partial recovery takes place. Shortening of the tendons and capsule of the shoulder-joint and about the other joints is present. In cases which do not completely recover subluxation of the shoulder-joint is often associated with birth palsy.

So far as treatment is concerned, as soon as possible after birth the arm must be fixed in a position to relax the paralyzed muscles. A splint or plaster-of-Paris brace is necessary. The splint consists essentially of a broad body piece and a narrow arm piece, suitably padded and furnished with webbing, straps, and buckles. This position of relaxation must be constantly kept up night and day. In addition daily massage and passive movements at the shoulder should be begun. When the patient begins to recover she must have exercise to train the muscles. Massage to be of use must be superficial and carried out with the muscles kept constantly relaxed. The splint must be used until the power of active external rotation and abduction at the shoulder has returned. If, after three months, the paralyzed muscles give the reaction of degeneration to electrical tests, operation should be performed. The writer does not speak enthusiastically of operation. As the nerves are small it is difficult to dissect them out completely and to close them accurately. Should anastomosis be made it must be at the periphery. As a rule these patients recover, for it is very rare to see an adult who shows the results of birth palsy in infancy. Where the shoulder is deformed by internal rotation and the case has been neglected for several months, the position of the head of the humerus should be carefully ascertained, and if no subluxation is present, an anesthetic should be given, the contracted capsule stretched and the limb placed in the position first used in a splint or plaster. If the capsule cannot be stretched, an open operation with division of the contracted tissues is indicated. Where there is posterior subluxation of the shoulder-joint, the effort should be made under anesthesia to reduce a subluxation by manipulation. Should this fail, after two years of age an open operation is indicated, approaching the joint by the anterior route and dividing the anterior capsule and subscapularis tendon. It may be necessary to partially remove the acromion. Plaster-of-Paris should then be applied. Fixation is indicated for three months, followed by massage and movements.

Complete Inversion of the Uterus, with Prolapse and Recovery.—STEWART (*Brit. Med. Jour.*, June 26, 1915) reports the case of a primipara, delivered with forceps without especial difficulty. The uterus contracted well, and ten minutes after the birth of the child the placenta was about to be expelled. When this was removed the uterus was found completely inverted. There was practically no hemorrhage, but the placenta was somewhat adherent. It was detached and the effort made under chloroform to reduce the inversion for twenty minutes. This was followed by profound collapse and the effort was abandoned. Under stimulation the patient slowly rallied and was removed to a hospital, where, under anesthesia, the inversion was reduced by taxis. The patient's convalescence was prolonged and complicated, but she finally regained complete health. In reviewing this case, it must be noted that the placenta is said to have been "somewhat adherent," and also that in ten minutes after the delivery of the child the placenta appeared in the vagina. We question very much whether there was any real adhesion of the placenta, but the abnormality lay in the fact that sufficient time did not elapse after the birth of the child, before efforts were made by the patient or the physician to remove the placenta. From twenty minutes to a half hour should elapse after the expulsion of the child, while the mother remains perfectly quiet, before efforts are made to deliver the placenta. The placenta does not separate immediately, and as in this case, there is sufficient cohesion between the placenta and uterine wall to favor the inversion of the uterus.

The Intolerance of the Fibroid Uterus to Twin Pregnancy.—MONTUORO (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) reports three cases of twin pregnancy, complicated by fibroids of the uterus, in which abortion had occurred or the patient had to be operated upon for hemorrhage with threatening symptoms. He has collected from the literature fifteen other cases, and his own experience and statistics show that when twin pregnancy occurs in the fibroid uterus but 27.07

per cent. go on to viability or near term; 16 per cent. abort and between 55 and 56 per cent. come to operation. The period of pregnancy in which abortion usually occurs varies from the third to the sixth month. Twin pregnancy seems to stimulate fibroids to very rapid growth, while on the other hand the growth of the embryos produce great distension of the uterus, especially in the tissues in the region of the fibroids. This paper is valuable in forming a decision as to the treatment of such a case. It is useless to wait for pregnancy to develop to full term and the rule should be that twin pregnancy and fibroid uterus is best treated by prompt hysterectomy.

The Treatment of Placenta Previa.—Stratz (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) in his Clinic at the Hague follows Schroeder and Hofmeier in his belief that combined version, followed by spontaneous labor or very slow extraction is the best treatment for placenta previa. He endorses in full Schroeder's statement that the best results in the treatment of placenta previa will be obtained if little consideration is given the interests of the child. By such a method infant mortality will not be excessive, while the maternal mortality willbe much lessened. Stratz has treated 173 cases, of whom the greater part were private patients. There were 63 cases of deep insertion of the placenta, in which hemorrhage ceased so soon as the membranes were ruptured. In 110 combined version was practised. He made no difference between central and lateral placenta previa, but made his diagnosis from the fact that on vaginal examination the os was practically filled with placental tissue. Of the 173, one mother in the Polyclinic practice died, a mortality of 0.6 of 1 per cent. This patient gave birth spontaneously, after version, to a living child, but a half hour after the placenta had been expressed, sat up in bed suddenly, collapsed and died. At autopsy an open sinus the size of a little finger was found in the uterus at the contraction ring. The hemorrhage preceding the patient's death was not excessive, and embolism was the most probable cause. In 50 patients there was moderate elevation of temperature. In 3 there was pronounced infection, 2 having purulent endometritis, 1 had pelvic abscess which ruptured spontaneously into the rectum. These 3 cases had been tamponed by the general practitioner in attendance. All three recovered. Seventy-seven of the children were stillborn, and 20 had been dead for some time before birth. This makes a total fetal mortality of 45 per cent. The writer quotes the statistics of placenta previa for the year 1914 in Holland. The number of cases reported is 881, with a maternal mortality of 7 per cent. and a fetal mortality of 43 per cent. In those clinics where combined version is used as a method of treatment, 236 cases are reported, with a maternal mortality of 2.7 per cent. and a fetal mortality of 68 per cent. Embolism is a not uncommon cause of death following placenta previa, probably because of the unusual development of bloodvessels in the lower portion of the uterus. Stratz believes that where the bleeding is slight, the patient should be put at absolute rest and given narcotics. The tampon should be completely abandoned as a method of treatment and interference practised as rarely as possible. Where hemorrhage is considerable, combined version bringing the child down sufficiently to check the hemorrhage, and if possible spontaneous expulsion should be procured. Under especially favorable circumstances, where the birth canal is dilated and the child not large, it may be very carefully extracted. The use of the dilating bag is unnecessary in most cases of placenta previa. Cesarean section he thinks is indicated only when a living child is earnestly desired, or in the presence of other complications.

GYNECOLOGY

UNDER THE CHARGE OF

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Etiology of Adnexal Inflammation.—In a recent article Neisser (*Med. Klin.*, 1915, xi, 511) calls attention to the fact that ever since the discovery of the gonococcus in 1879 some difference of opinion has existed between the andrologists—among which he classes himself—and the gynecologists as to the etiology of adnexal inflammations. He says truly that most gynecologists take the standpoint that when a hitherto healthy woman, whose husband has passed through an attack of gonorrhea at some previous time, develops within the first year or so of married life, or after her first pregnancy, an ascending endometritis and adnexitis, it goes without question that the latter is gonorrheal in origin, no matter how many repeated examinations of the husband have failed to demonstrate the presence of gonococci. Neisser says that he cannot agree with this viewpoint, for he believes that in many of these cases there may not be a true gonococcal infection. He says that this point has assumed a more practical interest than it formerly possessed since the introduction of modern immunotherapy, which requires for its successful application a determination of the specific organism at fault. He thinks that many of the failures reported from the use of gonococcal vaccines in cases of this type are probably due to the fact that the infection is not gonorrheal at all, but that other organisms may be responsible. These may be forced into the uterus by douches given under too high pressure. Moreover, it is well known, he says, that in every case of postgonorrheal urethritis in the male, quantities of bacteria of various kinds are harbored in the urethra long after the gonococci have entirely disappeared, and he suggests the possibility that in some cases some of these organisms may cause inflammation of the female organs. He admits that examination of organisms of this type has failed to show any marked pathogenicity so far as the ordinary laboratory animals are concerned, but this does not prove that they may not possess this property when in the human mucous membrane. He thinks the problem can be definitely solved only by careful and extensive bacteriological investigations by andrologists and gynecologists working together, but that in the meantime, we should be a little slower in jumping at conclusions that may mean the wrecking of a marriage until we are a little more sure of our ground.

Treatment of Carcinoma of the Uterus by the Percy Cautery.—This method of treatment for inoperable carcinoma of the cervix consists, as we brought out in discussing it a few months ago, in the utilization of a heavy cautery, of not sufficient heat to cause any charring of the tissue, but merely to thoroughly cook the whole area, as it were, by a degree of heat high enough to destroy malignant cells, without devitalizing healthy tissue. Heretofore most of the literature upon the subject has come from Percy himself, but a recent article by Balfour (*Jour. Lancet*, 1915, xxxv, 347) gives a preliminary report on 31 cases treated at the Mayo Clinic from January 1914 to June 1915. As Balfour emphasizes, of course nothing can be said as yet as to end-results in these cases, but the immediate effects have been so favorable that he feels the method has a very distinct field of usefulness. In all the patients there was immediate cessation of bleeding and discharge, with corresponding improvement in the general condition. Upon reëxamination six weeks to three months after operation, one generally finds a greatly increased mobility of the uterus, with an atrophic, clean, smooth cervix and vaginal vault. So far Balfour has not, as a rule, considered it advisable to give more than one cauterization treatment in each case. In nine instances a radical hysterectomy was subsequently performed, and in five of these careful pathological examination of the removed specimen failed to reveal the presence of any malignant tissue. The author admits the possibility that in some of these a primary hysterectomy might have been done, but he considers the preliminary heating of undeniable value in borderline cases. Destruction of the cancer cells themselves is not the only advantage of this: in from two to three months the shrivelled cervix in a scarred, firm vaginal vault, which has resulted, makes it possible to do a much cleaner and more satisfactory operation; the foul, infected tissues of the cancerous cervix are sterilized, and the very important factor of bacterial infection, which is largely responsible for the primary mortality of this operation, is removed. In a few cases complications were encountered, such as vesical fistulæ, late secondary hemorrhage, and implantation metastasis in the vagina. With increasing experience in the technique, however, Balfour thinks that most of these may be avoided. In the latest publication on the subject by Percy himself (*Amer. Jour. Obst.*, 1915, lxxii, 298) many interesting and important details of his technique are described, with numerous illustrations of his instruments and method of arranging the patient for the vaginal and abdominal work. Percy does not hesitate to repeat the cauterization four or five times on the same patient, if necessary, opening the abdomen each time to control by palpation, the amount of heat being disseminated through the uterus and adjacent structures. This he considers to be an absolute *sine qua non*, if satisfactory results are to be obtained. He says that he now routinely ties both internal ialiac arteries, to aid in starvation of the growth. and to prevent the danger of secondary hemorrhage which previously occurred in several cases.

DERMATOLOGY

UNDER THE CHARGE OF

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A Tumor-like Form of Lupus.—Fischer (*Dermat. Ztschr.*, April, 1915) reports an unusual case of lupus, characterized by numerous tumor-like lesions, occurring in a young Russian, twenty-two years old, who was at first suspected to be suffering from leprosy. The left leg, which was notably enlarged and elephantiasic in appearance, was the seat of numerous discrete and confluent tumors varying in size from a pea to a cherry, and many cicatrices. The histological and bacteriological study of the case demonstrated its tuberculous nature. The cutaneous affection was most probably secondary to an osseous tuberculosis of the leg beginning inchildhood. Fischer insists upon the strict separation of these tumor-like cases from other forms of cutaneous tuberculosis, such as the papillomatous proliferations which occasionally occur in ulcerating lupus, tuberculosis verrucosa cutis and lupus verrucosus, with which they have nothing to do.

Congenital Familial Hereditary Alopecia the Result of Hypothyroidism.—Petersen (*Dermat. Ztschr.*, April, 1915) reports an example of hereditary alopecia occurring in three generations, affecting equally the male and female members of the family, and limited strictly to the scalp. The affected individuals were born with a normal growth of hair which continued to grow normally until about the fourth or sixth year. It then began to fall out and lose its pigment, becoming completely colorless, and continued to do so until at puberty or a little later the scalp was completely bald. In three children of the family under Petersen's observation the administration of thyreoidin, in doses of 3 to 9 centigrams daily, was followed by good results. After about eight months of this treatment the hair ceased to fall and regained its color. The favorable result following the administration of thyreoidin leads Petersen to conclude that the affection was due to deficient endocrine secretion the result of diminished activity of the thyroid gland.

Pemphigoid Eruptions Following Vaccination.—Mook (*Jour. Cutan. Dis.*, October, 1915), in an interesting paper on this important subject, sums up the result of the study of his own cases and of those in literature as follows: The cases may be divided into three groups: (A) those which terminate in rapid recovery and may or may not be accompanied by constitutional disturbance; (B) those which continue as a chronic recurrent vesicular or bullous affection which may or may not be accompanied by constitutional disturbance; (C) a third group which terminates rapidly in death. The period of incubation varies from three or four days to four months, the average period being in the majority of cases from three to five weeks. In the benign cases the bullæ are smaller than in the severe ones. The eruption shows a predilection for the neighborhood of the mouth, the neck, and extremities, particularly the joints. Inoculations in monkeys, a calf, guinea-pigs and rabbits were negative. Blood cultures from a fatal case and from two which recovered were negative under various conditions and on various media. Ordinary staphylococci were obtained from cultures made from the contents of some of the bullæ while others were found sterile.

Trichloracetic Acid and its Uses in Dermatology.—Davis (*Jour. Cutan. Dis.*, October, 1915) thinks trichloracetic acid has a selective action upon epithelial tissues and finds it most useful in the treatment of a number of cutaneous affections where a somewhat superficially acting cauterant is indicated. In patches of degenerative seborrhea and in pigmented moles its use is followed by satisfactory results. The skin is cleansed with benzine to facilitate the penetration of the acid which may be applied with a toothpick wrapped with a bit of cotton. It is particularly useful in pigmentations, papillomata and nevi. In xanthoma palpebrarum Davis regards it as the ideal remedy. In fissures in the region of the mouth and nares and about the anus he has found it invaluable.

The Relation of Animal to Human Sporotrichosis.—Meyer (*Jour. Amer. Med. Assn.*, August 14, 1915), since 1911, has been investigating the reported cases of the transmission of sporotrichosis from the horse to man, most of the work being done in Pennsylvania where sporotrichosis in horses is a common affection. The evidence which he collected does not support the theory that the malady is very frequently transmitted from the horse to man. Only two cases of human sporotrichosis have been recorded in Pennsylvania, and in one of these infection by contact with a sporotrichotic horse was at first suggested but could not be proved conclusively. The absence of the affection among veterinarians and farmers in Pennsylvania where it is very common in the horse demonstrates, in Meyer's opinion, that sporotrichotic infection in man by contact with the horse occurs only very rarely.

Lupus Erythematosus of the Mucous Membranes.—Culver (*Jour. Amer. Med. Assn.*, August 28, 1915) reporting eleven cases of lupus erythematosus affecting various mucous membranes, announces it as his belief that the mucous membrane lesions as well as those upon the skin are the result of a general disease, the evidence pointing to digestive and assimilative faults as the most important causes. He concludes that internal treatment and a proper regimen are quite as necessary as local treatment. In the discussion which followed the reading of the paper Pusey expressed his belief that lupus erythematosus is a toxic dermatosis, belonging in the erythema multiforme group.

Bullous Dermatitis Caused by the Colon Bacillus.—Potter (*Jour. Cutan. Dis.*, April, 1915) reports the case of a young woman who one month after a normal labor was seized with convulsions, the origin of which could not be determined. During the patient's second week in the hospital an erythema appeared on the arms and face which disappeared in the course of three or four days except upon the face where it persisted. A bullous eruption then appeared upon the hands, forearms and ankles accompanied by slight elevation of temperature (101°). Nothing abnormal was found in any of the viscera, and smears taken from the cervix and vagina shows nothing. Cultures made from the contents of the blebs revealed a type of the colon bacillus. The bullous eruption spread to the face, shoulders, buttocks and lower limbs, and new lesions continued to appear throughout the course of the illness which lasted about six weeks, running an irregular course similar in some respects to typhoid fever, but the Widal reaction was repeatedly negative. The treatment consisted in the employment of an autogenous vaccine which Potter thinks was of benefit in checking the appearance of the blebs.

Paraphenylene Diamene Dermatitis.—BUNCH (*Brit. Jour. Dermat.*, September, 1915) has recently had under his care a number of cases of a severe dermatitis resembling in appearance a weeping eczema, situated upon the scalp and face resulting from the use of paraphenylene diamene used as a hair dye. In severe cases the dermatitis affects the entire face and may spread to the chest and back. While this dermatitis may follow the first application it may not appear until it has been applied a number of times. (I have seen a number of cases of a like kind in the past year in all of which the cause was entirely overlooked, no suspicion being entertained by the patient or her physician that the dye had anything to do with the dermatitis which was supposed to be an eczema.—M. B. H.)

Etiology of Erythema Nodosum.—ROSENOW (*Jour. Cutan. Dis.*, May 1915), at the clinical session of the 38th Annual Meeting of the American Dermatological Association, demonstrated cultures of a markedly pleomorphic organism obtained from the subcutaneous nodes in six typical cases of erythema nodosum, which he believes to be the cause of the disease. The same organism was also obtained from a cervical gland draining an infected tonsil in one case, from the focus of infection (tonsil and superficial ulcer on the anterior pillar) in two cases, and from the blood in pure cultures in two cases. Injected intravenously into dogs, rabbits and guinea-pigs, it exhibits a remarkable affinity for the subcutaneous tissues, producing localized subcutaneous hemorrhages followed by infiltration, migration of leukocytes, and enlargement of neighboring lymphatic glands. The hemorrhages are frequently symmetrically distributed, and from the hemorrhagic areas the organism has been isolated repeatedly. In smears from original colonies the organisms presents all gradations between bacilli, elongated diplococci and cocci, the form probably depending upon conditions of environment.

The Vaccine Treatment of Ringworm of the Scalp.—STRICKLER (*Jour. Cutan. Dis.*, March, 1915) reports seven cases of ringworm of the scalp cured by injections of a vaccine prepared by growing the infecting organism upon "French Proof Agar" in an Erlenmyer flask, triturating the cultures thus obtained with crystals of chemically pure sodium chloride and afterward adding enough sterile distilled water to make a normal salt solution. The vaccine was preserved by the addition of 0.25 per cent. phenol. The dose varied from 1 c.c. to 2 c.c. given at intervals of three days. After the patient has had 6 or 7 injections an infiltrated area appeared in some cases at the site of the injection about thirty-six hours after it. In one case abscesses followed the injection of the vaccine and the treatment had to be discontinued. The number of injections varied from seven to seventeen. Strickler concludes from his experience with these cases that ringworm of the scalp can be cured by vaccines, but is not prepared to state in what proportion of the cases treated a cure can be obtained in this manner.

PATHOLOGY AND BACTERIOLOGY

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Nature and Clinical Importance of Pseudodiphtheria Bacilli.—Numerous workers have called attention to the finding of organisms closely resembling B. diphtheriæ, in various parts of the body. Such organisms have now been recognized as normal inhabitants of the nose, throat, ear, genitalia and skin. Under such conditions these bacteria have no significance. But the question whether these organisms can be important factors in disease processes under abnormal conditions is far from clear. Fox (*Jour. Med. Research*, 1915, xxxii, 309) has made a study of the diphtheroids in an attempt to throw some light upon their relationship to disease. Four groups of organisms are commonly recognized: (1) true diphtheria bacilli; (2) avirulent members of group one; (3) pseudodiphtheria organisms which morphologically resemble group one and two, but differ culturally and (4) organisms belonging to the so-called Hoffman group which, although bearing a basic resemblance to the above three groups, differ both morphologically and culturally. The last group has also been spoken of as pseudodiphtheria. Not a little importance has been placed upon the various members of the pseudodiphtheria bacilli in crediting them with peculiar pathogenic qualities. Thus some importance has been placed upon their presence in otitis media, vaginitis, coryza and lesions of the lymphatic glands. In all instances where the organism is found in external ulcers it is in mixed culture. Pure cultures, however, have been isolated from the blood, spleen, lymph glands and body cavities at autopsy. The reports of these findings are in the majority of cases not clear in indicating the pathogenic qualities in man. The author expresses a desire for more thorough tests and studies of the pseudodiphtheria organism when isolated from conditions in which they appear an important etiological factor. Immunity tests and sugar reactions are particularly called for. The author points out that the results reported in Hodgkin's disease by various authors are not uniform and evidence is not available that the organisms isolated and reported are the same. With the wide-spread dissemination of members of the pseudodiphtheria group, their presence in mixed infections has been looked upon with little importance. Fox reports the isolation of these bacteria from 20 different cases, in only one of which did it appear to have an important bearing. In the majority of instances the organisms gain entrance to the body by the respiratory and genito-urinary tracts. Existing as saphrophites upon the mucous membranes they probably continue a non-parasitic or symbiotic existence in the animal body. What relation these pseudodiphtheria bacilli may bear to the avirulent B. diphtheriæ, is not known. The author was unable to bring about mutation of the true B. diphtheriæ by methods of culture.

Tumors of the Parathyroid Glands.—There have been relatively few reports of parathyroid tumors, the majority of which have been found by accident at autopsy. In only a few instances did they cause symptoms of a character that would have a bearing upon the functions of the glands. HARBITZ (*Jour. Med. Research*, 1915, xxxii, 361) has collected the cases in the literature, the first of which was reported by De Santi in 1900. The author points out that all of the tumors reported cannot be acepted as of parathyroid origin. Not a few of them are described in intimate association with the thyroid. The author adds 2 new cases of parathyroid tumors, one of which was associated with osteomalacia and the other with paralysis agitans. In view of the work of McCallum on the increased calcium output in disturbances of parathyroids this association with osteomalacia is very significant. The presence of parathyroid disease in paralysis agitans has previously been observed by other Norwegian authors.

Splitting of the Elastic Fibers in Arteries.—In the pathological classification of arteriosclerosis not a little weight has been placed upon the minute histological findings in diseased arteries. The alterations observed in the elastic tissue of arteries have constantly attracted attention until Jores, in 1903, gave an over-important place to this finding. According to him, and his views have been widely propagated in text books, the splitting of the internal elastic lamina in arteries was a process associated with hyperplasia of the musculo-elastic layer and their presence in an artery indicated true arteriosclerosis. At that time it was pointed out that these organic changes in muscle and elastic fibers were prone to show degenerative changes of a fatty nature. Jores claimed that the splitting of internal elastic lamina was only obtained in the presence of contiguous muscular hyperplasia. In this study by McMEANS (*Jour. Med. Research*, 1915, xxxii, 377) it is shown that such splitting may occur in the absence of muscle changes and are found in the vicinity of inflammatory processes. Arteries obtained from inflammatory lesions of diphtheria, septicemia, typhoid fever, pneumonia, and chorea were all shown to have developed a splitting of the internal elastic fiber. A similar result was observed in the neighborhood of endothelial proliferative responses where fatty streaks of the intima were present. It is thus shown that the nature of this lesion is not specific as was claimed by Jores. Thus if the splitting of the elastic lamina is a characteristic of one of the types of arteriosclerosis the etiological factors bringing it about are multiple.

Spontaneous Rupture of the Kidneys in Acute Toxic Nephritis.—Rupture of the kidney is usually a surgical condition of traumatic origin. Spontaneous rupture on the other hand is an infrequent process resulting from a slowly progressive pathological condition within the organ itself. In all, some 30 cases have been reported. Perirenal hemorrhage is obviously a constant finding. This hemorrhage may result from renal arteriosclerosis, interstitial nephritis and acute parenchymatous nephritis or from renal neoplasms, tuberculosis, abscess and infarct. The case reported by Wade (*Jour. Med. Research*, 1915, xxii, 419) was one of a negro of twenty years with acute parenchymatous nephritis. Both kidneys were markedly swollen with multiple ruptures through the capsule. Curiously enough no symptoms indicated this serious damage during life.

Thyroid and Circulatory Changes following Experimental Ligation of the Thyroid Vessels.—Newhof (*Jour. Med. Research*, 1915, xxxii, 501) experimented upon dogs to determine the effect of ligation upon the thyroid. He points out that much care must be taken in the interpretation of the results in that the histology of the thyroid is far from uniform and that certain traumata induced during the operative procedure are apt to bring forth organic changes not dependent upon the vascular occlusion. Uniform results do not follow the ligation of the thyroid arteries or veins. More marked effect was obtained upon ligation of the veins than of the arteries. At the end of several months the alveoli are increased in size, while some increase of connective tissue may be observed. The interference with the arterial supply showed mainly a diminution in the size of the acini. In general, the results obtained by the author are so slight that this method of operative approach for the enlarged thyroid does not appear very encouraging.

The Origin of Local Eosinophilia.—The presence of a local eosinophilia in tissues is not an uncommon observation. It is most commonly seen in certain specific infections, chronic granulation tissue, and peculiar lesions such as are found in anaphylaxis. Considerable controversy has developed as to the origin of these eosinophiles. Some claim they migrate from the hemopoietic organs, others that they arise locally from mixed tissue cells of the injured part. Photakis (*Ztschr. f. Exper. Path. u. Therap.*, 1915, xvii, 270) studied the development of local eosinophilia in anaphylactic shock. Under these conditions it has been repeatedly found that the lungs have become the site of great accumulations of eosinophiles. The author found that the sensitizing dose, using serum, did not alter the numerical cellular state, nor did bone-marrow show any change at the moment before the active anaphylactic dose was given. Having furthermore treated the animals with intravital strains, he was able to show that the local tissues in the lungs played no part in the production of the eosinophilia subsequently developing in it. He was also able to observe the direct migration of the eosinophiles into the interstitial tissues from the lung capillaries. Quite marked cellular changes indicative of an overproduction of eosinophiles occurred in the bone-marrow.

Bacteria of Plant Tumors as Causative Agents of Human Disease.—FRIEDEMANN, BENDIX, HASSEL and MAGNUS (*Ztschr. f. Hygiene*, 1915, lxxx, 114) believe that they have established an animal and vegetable pathogenicity for the B. tumefaciens. On four separate occasions they isolated a Gram-negative bacillus (actively motile, showing acid on litmus whey, acid and gas on dextrose and lactose, no fermentation of saccharose, liquefaction of milk and a luxurient shiny growth on agar) from a case of suppurative arthritis and 3 cases of suppurative meningitis. These organisms have the biological characters of B. tumefaciens, as described by Smith and Jensen. The serum reactions, however, of one of the strains differs markedly from the others, as well as from the Jensen organism. This aberrant strain they claim agreed with the reactions of another strain of B. tumefaciens. They believe that there are two types of this organism distinguishable only through the serum reaction. In 2 of their cases of meningitis they observed the presence of meningococcus in direct smears but were not able to isolate them on their cultures and the organisms subsequently isolated had not been observed in the direct smears. The organisms obtained from the human did not produce any type of tumor growth in plants. All of the cultures had more or less pathogenicity for small animals. A similar organism has been isolated from the feces of those suffering from colitis.

Phagocytic Properties of the Eosinophile and the Absorption of Toxic Products of Vermes.—The phagocytic property of eosinophiles is well established and has been studied by various authors. WEINBURG and SEQUIN (*Ann. de l'Inst. Pasteur.*, 1915, xxix, 32) have taken up the study of the importance of this phagocytosis and also the conditions under which it manifests itself. The authors studied the action of the eosinophile in the role of the phagocyte both *in vitro* and *in vivo*. *In vitro* they observed its reaction toward (1) inert substances; (2) various bacteria; (3) protozoa; (4) red blood cells. They found that the eosinophiles possess the power of engulfing inert materials and also of phagocyting the majority of bacteria as well as protozoa and red blood cells. Many of the bacteria, protozoa and red cells were completely digested by the eosinophiles. *In vivo* the authors studied phagocytosis by the eosinophiles in the peritoneal cavity, in the adjacent subcutaneous tissue, and in the circulating blood of the guinea-pig. They found that the phenomenon takes place with equal readiness in each of these situations and when the eosinophiles are very abundant in the blood or when they are massed together at the point of entrance of the bacteria they play an important part in protecting the organism from infection. However, these eosinophiles play only a secondary role in phagocytosis as their presence is rather infrequent in purulent collections. Sufficient recognition is not accorded the eosinophile because the bacteriological staining technique does not usually permit of the differentiation of the various kinds of leukocytes. A third seires of experiments was undertaken to demonstrate the inhibition of phagocytosis by the use of the liquid from hydatid cysts. The eosinophiles, having been subjected to the hydatid liquid for an hour at 37°, no longer showed evidence of their phagocytic qualities, although the other leukocytes retained their power of engulfing organisms. The authors state that eosinophiles from immunized animals absorb the hydatid antigen more readily than do those of normal animals. They conclude that the eosinophile leukocytes play an important role in immunity and are especially adapted to neutralizing toxic substances of certain parasites.

Primary Melanosarcoma of the Adrenals.—Maclachlan (*Jour. Med. Research,* 1915, xxxiii, 93) gives a description of an unusual tumor of the adrenal occurring in a male of forty-eight years. The tumor was a bilateral melanosarcoma with extensive metastases. Macroscopically the tumors were roughly triangular in shape, somewhat suggestive of the normal adrenal and almost equal in size (measurements 10 x 8 x 4 cm.). The primary and secondary growths were all intensely pigmented. There was no trace of normal adrenal either in the gross or in microscopic sections. In discussing the origin of the tumor the author concludes that there was a primary site in both adrenals arising from chromatophore cells which were probably congenitally aberrant. The absence of any bronzing of the skin and mucous membranes with complete destruction of the adrenals was emphasized. The skin, in fact, appeared pale and of a leaden color. The possibility of the sympathetic ganglia taking on the adrenal function with the prevention of pigmentation in the skin as is sometimes seen in Addison's is considered as an explanation, but another hypothesis is offered. The amount of pigment formed by the primary tumor and its secondaries is excessive, and possibly accounted for all the melanin which was being produced. It would appear further that the tumor cells had greater power to produce melanin than the skin. The author takes for granted that the pigmentation of the skin seen in Addison's disease is due to substances of the melanin group.

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